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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 28 1950

PRODUCTION OF HYPERTENSION AND HYALINOSIS BY DESOXOCORTISONE

BY

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[WITH SPECIAL PLATE]

A few years ago we observed that, in animals, overdosage with desoxycorticosterone reproduces the experimental equivalent of certain hypertensive, rheumatic, and allergic diseases of man—in particular, malignant nephrosclerosis, necrotizing arteritis similar to periarteritis nodosa, cardiac nodules resembling Aschoff bodies, joint lesions comparable to rheumatic or rheumatoid arthritis, as well as an intense and persistent rise in arterial blood pressure. All these changes were most readily observed in animals sensitized to these toxic actions of DCA-overdosage by unilateral nephrectomy and a high sodium intake. Essentially the same changes developed in similarly sensitized animals if we exposed them to a variety of noxious agents capable of producing a general-adaptation syndrome with the characteristic stimulation of the adrenal cortex. Since in man these diseases are often preceded by exposure to cold, infections, intoxications, or other damaging agents, we expressed the opinion "that the above-mentioned diseases are, at least partly, caused by an abnormal (probably excessive) adaptive response of the adrenal cortex and represent diseases of adaptation" (Selye and Pentz, 1943).

It has been noted, furthermore, that DCA causes arthritis more easily in adrenalectomized than in intact animals (Selye *et al.*, 1944; Pirozynski and Akert, 1949), and that a gluco-corticoid compound (corticosterone) increases, while a mineralo-corticoid substance (desoxycorticosterone) diminishes, resistance to traumatic shock (Selye, Dosne, Bassett, and Whittaker, 1940).

Subsequent investigations revealed that the arthritis (Selye, 1949a), the anaphylactoid reactions (Selye, 1949b), as well as the cardiovascular and hypertensive changes (Selye, in press), whose development is enhanced by desoxycorticosterone, can also be inhibited by cortisone. All these observations led us to formulate the working hypothesis that, as a result of exposure to stress (for example, that caused by emotional stimuli, infections, intoxications), the adrenal may, under certain circumstances, respond with a disproportionate over-production of either the gluco- or the mineralo-corticoids. The above-mentioned diseases of adaptation could perhaps be the result of an unbalanced excess of the latter type of steroid.

The most serious objection raised against this kind of reasoning was that desoxycorticosterone has not been definitely proved to be produced by the adrenal cortex. It has only once been isolated from suprarenal glands (Reichstein and von Euw, 1938), and some chemists expressed the suspicion that this may have been an artifact (for literature, see Selye, "Stress"). Of course Hartmann's "sodium factor" and Kendall's "amorphous fraction" possess mineralo-corticoid potency, and these are indubitably natural adrenal steroids; but the latter compounds have not been available in the quantities required to examine whether they would actually produce lesions characteristic of the above-mentioned "diseases of adaptation."

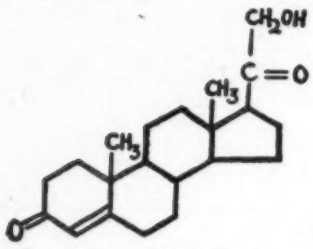
Using certain impure anterior-pituitary preparations, we found that hypertension, periarteritis nodosa, cardiac nodules, nephrosclerosis (Selye, 1944), and arthritis (Selye, 1946, 1949a) are produced simultaneously with a pronounced adrenocortical enlargement. However, these extracts contained much foreign protein, and hence there still remained some doubt concerning the mechanism through which they produced these changes. In particular, the question has been raised whether both desoxycorticosterone and our impure extracts could not have acted merely by eliciting allergic responses if they are toxic substances foreign to the body.

In view of these uncertainties we felt that it would be of fundamental importance, for the interpretation of the "diseases of adaptation," to demonstrate that an unquestionably natural mineralo-corticoid can also produce them. This has now become possible, and in this communication we should like to report upon the results of our pertinent observations.

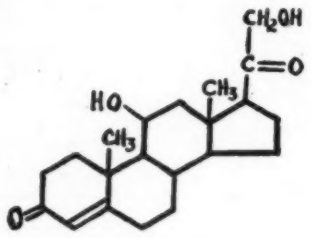
The mineralo-corticoid with which this work was performed is Reichstein's compound "S" or 11-desoxocortisone. It bears nearly the same relationship to cortisone as desoxycorticosterone to corticosterone. For the discussion of the problem under consideration it is unnecessary to devote much space to the chemistry of these steroids, but it will facilitate the understanding of our subject to list the structural formulae of the principal compounds to which reference has been made.

It will be noted that desoxycorticosterone and desoxocortisone differ from corticosterone and cortisone, respectively, only in that the former two steroids do not possess an oxygen on carbon atom 11. The presence of oxygen in this position is indispensable for the gluco-corticoid actions (Selye, 1943, Selye, Dosne, Bassett, and Whittaker, 1940). In corticosterone it is a hydroxylic (hence the prefix "desoxy-"), in cortisone a ketonic (hence "desoxo-"), oxygen that is removed.

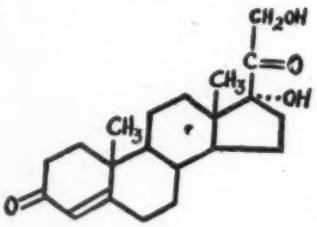
We were especially interested in determining whether desoxocortisone would produce the diseases of adaptation



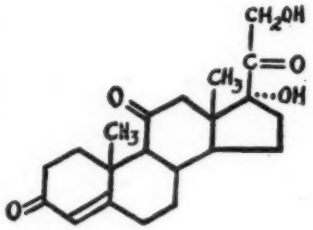
Desoxycorticosterone



Corticosterone



Desoxocortisone
(Reichstein's compound " S ")



Cortisone

of the " hyalinosis " type because it is so closely related to cortisone, which inhibits the progress of these same diseases both in clinical and in experimental medicine (for literature, see Selye, 1949a). Furthermore, cortisone has repeatedly been isolated—in comparatively large amounts—from normal adrenal tissue (Reichstein, 1938, Reichstein and von Euw, 1938, 1940).

Methods

The experimental animals used in this study were immature male piebald rats, with an initial body-weight of 40–60 g. All animals were castrated and unilaterally nephrectomized at the beginning of the experiment. Throughout the period of observation they were fed exclusively on " purina fox chow " (as supplied by the Ralston Purina Co., Montreal) and given 1% NaCl as a drinking-fluid instead of tap-water to drink.

Young animals were used, because our supply of desoxocortisone is very limited and we felt that the greatest effect could be expected from a given dose in small rats. Gonadectomy was performed, since this permitted us, simultaneously with the main investigation, to determine whether desoxocortisone has any testoid (or " androgenic ") effects, as judged by the stimulation of the seminal vesicles, prostates, and penis. The unilateral nephrectomy and the administration of excess sodium served to " condition " the rats for the toxic actions of mineralo-corticoid overdosage.

Five rats received desoxocortisone as a saline suspension of desoxocortisone acetate microcrystals. The preparation was that distributed by Merck and Co., Rahway, N.J., in which suspending agents (to keep the microcrystals from settling) and 1.5% benzyl alcohol (as a preservative) are added. This suspension contains 25 mg. per millilitre, and 2.5 mg. was given daily subcutaneously to each animal.

For the statistical evaluation of the data the standard errors were calculated by the equation:

$$SEM = \sqrt{\frac{d^2}{n\,(n-1)}}$$

To calculate the organ-weight/body-surface ratio, the constant 9.1 was employed in the formula : $S = K \times W^{\frac{2}{3}}$, where S is the surface area in cm.², K is the constant, and W the body-weight in g. " P " was calculated according to Fisher's " t " table (1936).

The blood pressure was measured with the tail-cuff method, under very light ether anaesthesia, on the 22nd day of treatment, and all animals were killed two days later. The organs were preserved in alcohol–formalin mixture and weighed immediately after fixation. For histological examination they were embedded in paraffin and stained with haematoxylin and eosin.

Experimental Observations

To facilitate the evaluation of our data the main findings have been summarized in the following Table, in which—wherever it appeared of interest—the standard errors, and the probability of the statistical significance of the deviation from the normal (" P "), have also been listed. In the case of the kidney, heart, and brain, the organ weights are expressed both in absolute terms and as a function of the body surface. Statistically significant deviations from the norm are indicated in bold type.

TABLE I.—*Principal Changes Occasioned by Desoxocortisone Overdosage*

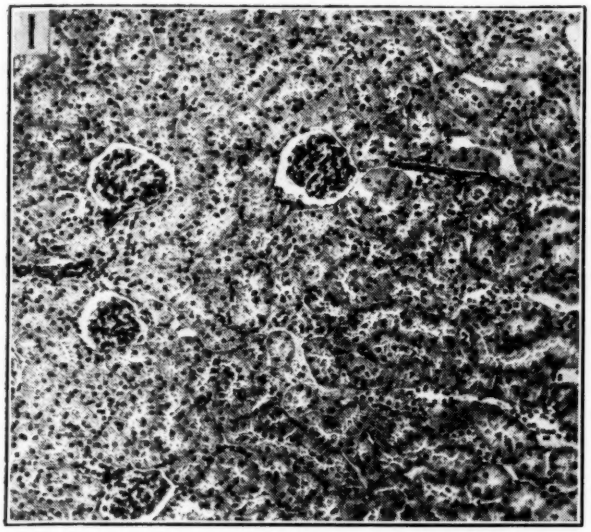
Treatment		Control	Desoxocortisone	" P "
Body weight in g.	Initial	54 ± 2	54 ± 1	—
	Final	132 ± 6	123 ± 7	—
Blood pressure (mm. Hg.) ..		125 ± 5	**150** ± 6	**<0·01**
Fluid intake (ml./day)		45 ± 2	**59** ± 2	**<0·01**
Kidney	in mg.	871 ± 55	1,001 ± 64	**>0·2**
	mg./100 cm.² B.S.	374 ± 30	447 ± 17	**>0·1** 5
	Nephrosclerosis	0	+ + +	—
Heart	in mg.	530 ± 32	**679** ± 15	**<0·0**.
	mg./100 cm.² B.S.	233 ± 14	**305** ± 10	**<0·0**?
	Myocarditis ..	0	+ + +	—
Brain	in mg.	1,265 ± 47	**1,450** ± 32	**<0·01**
	mg./100 cm.² B.S.	543 ± 34	**653** ± 37	**<0·1**
	Encephalopathy	0	+ +	—
Mesenteric periarteritis nodosa ..		0	+ + +	—
Thymus (mg.)		400 ± 37	307 ± 85	**>0·2**
Iliac lymph nodes (mg.) ..		26 ± 3	39 ± 7	**>0·2**
Spleen (mg.)		998 ± 63	1,045 ± 439	—
Adrenal (mg.)		29 ± 2	30 ± 1	—

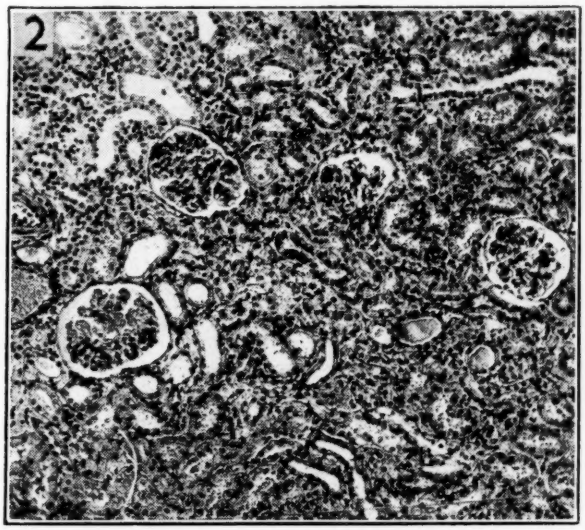
The body-weight of the experimental animals lagged only slightly behind that of the controls in spite of the widespread organ damage. This agrees with our previous observations, which revealed that only the gluco-corticoids cause sufficient tissue catabolism and inhibition of growth to depress the body-weight markedly. Nevertheless, probably the loss of weight was greater than the figures in our table would suggest, since the desoxocortisone-treated rats developed considerable tissue oedema, and this would mask their failure to grow.

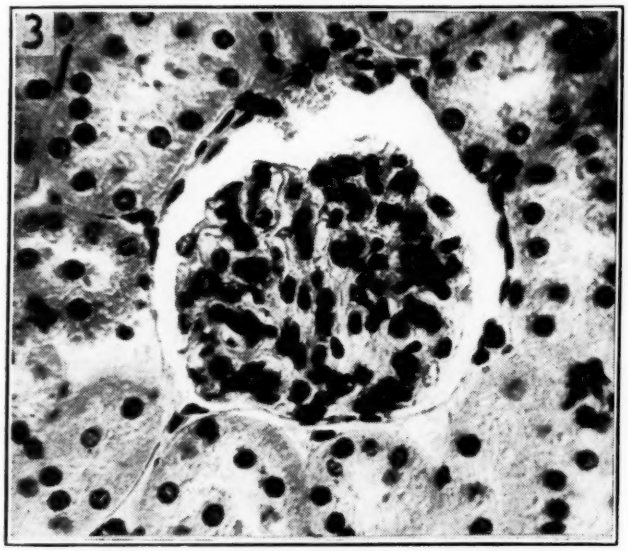
The blood pressure was measured and found to be significantly above normal on several occasions. This was also the case two days before necropsy, as shown by the figures listed in the table. It will be noted that our method measures the mean blood pressure and that in several of our animals this value was well over 160 mm. Hg. In normal rats the mean resting blood pressure measured under similar conditions does not rise over 135 mm. Hg.

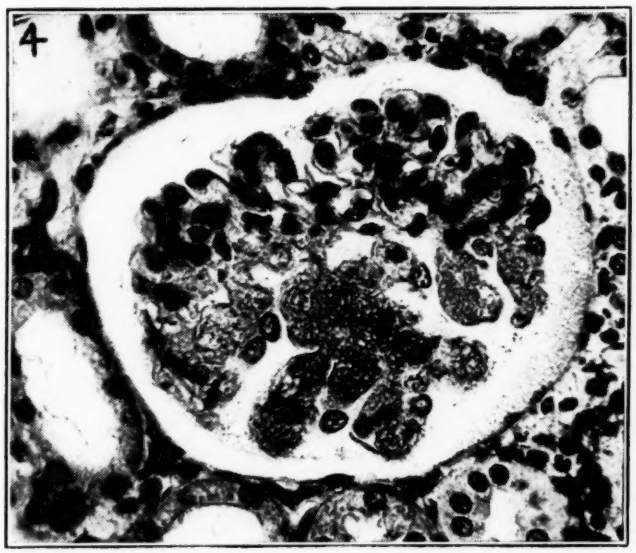
In order to obtain data concerning the water turnover it is more accurate to measure the intake than the output in experiments on the rat The figures given in the table represent averages of such measurements taken during the last twelve days of the experiment. It will be noted that, although desoxocortisone significantly raised the fluid intake, this increase was much less pronounced than that which we have previously observed in rats in which a similar degree of organ damage was produced by desoxycorticosterone (Selye, in the press). Nevertheless it may be concluded that desoxocortisone also possesses a diuretic effect.

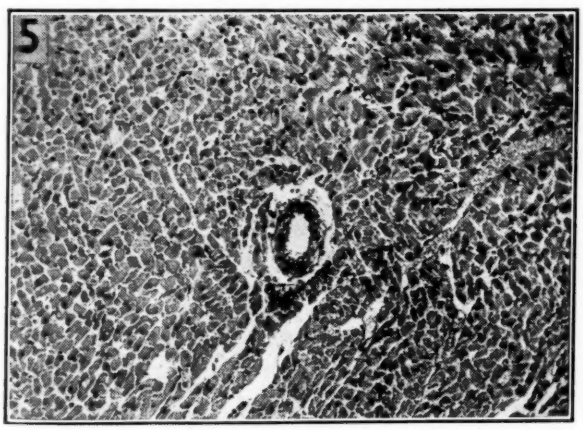
The weight of the kidneys was not significantly raised by desoxocortisone, when expressed either in absolute terms or as a function of body surface. On the other hand, histologically, all the treated animals showed marked nephrosclerosis, with hyalinization of many glomerular loops and











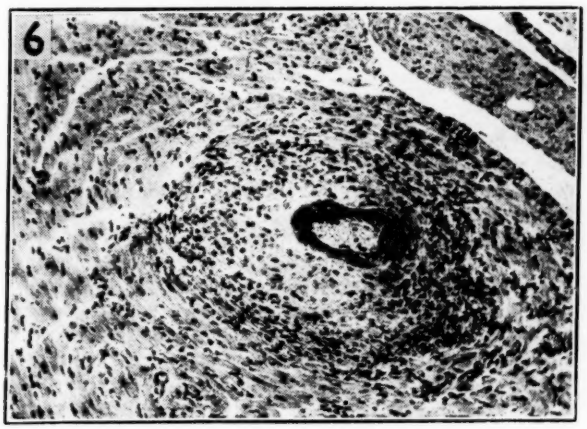


FIG. 1.—Kidney of a normal rat under low magnification.

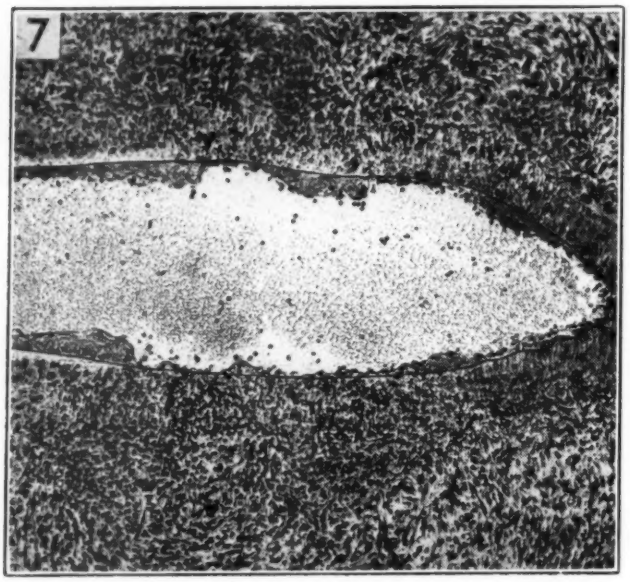
FIG. 2.—Kidney of a desoxocortisone-treated rat under low magnification: enlargement and hyalinization of some glomeruli; irregularity of tubules, some dilated and containing casts, others collapsed.

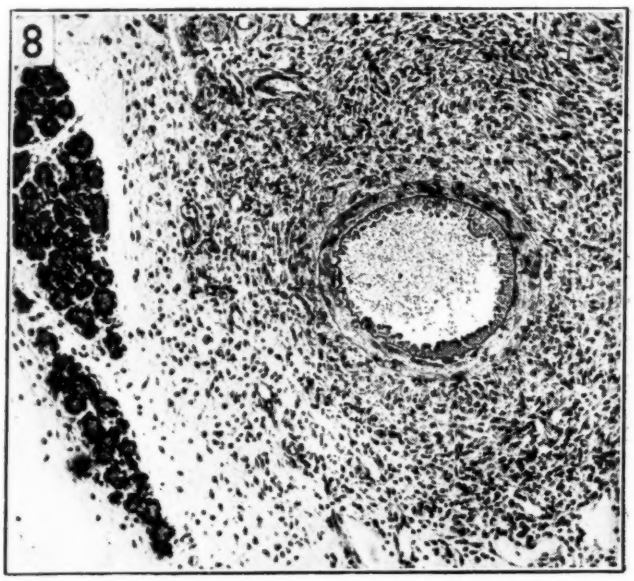
FIG. 3.—High magnification of a glomerulus from the kidney shown in Fig. 1.

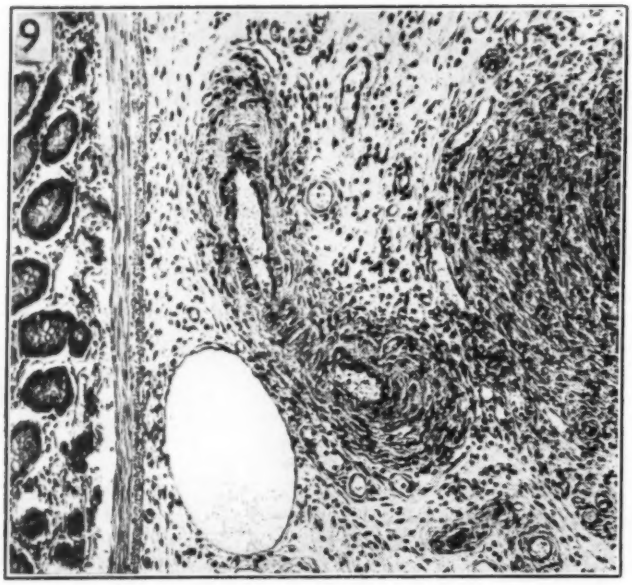
FIG. 4.—High magnification of a glomerulus from the kidney shown in Fig. 2 : hyalinization of several glomerular loops and dilatation of surrounding tubules.

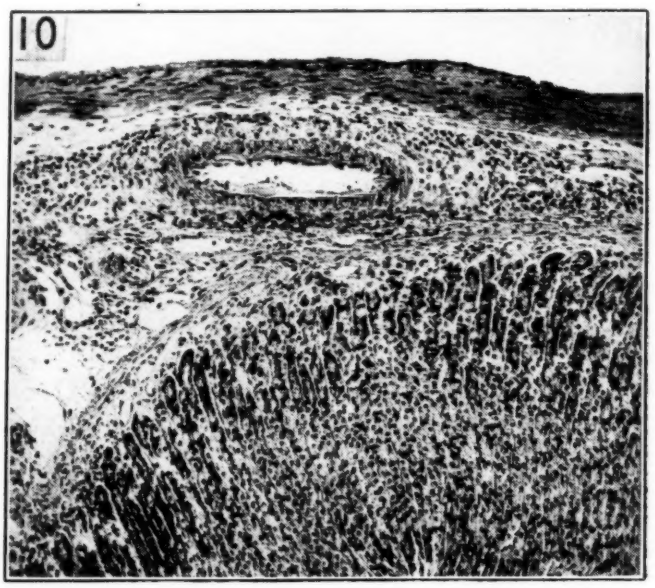
FIG. 5.—Arteriole in the myocardium of a normal control rat.

FIG. 6.—Arteriole in myocardium of a desoxocortisone-treated rat: although the lumen of this vessel is approximately the same size as that in Fig. 5, there is a heavy dark layer of hyalin material underneath the intima, and the outer walls are greatly thickened by a granuloma.









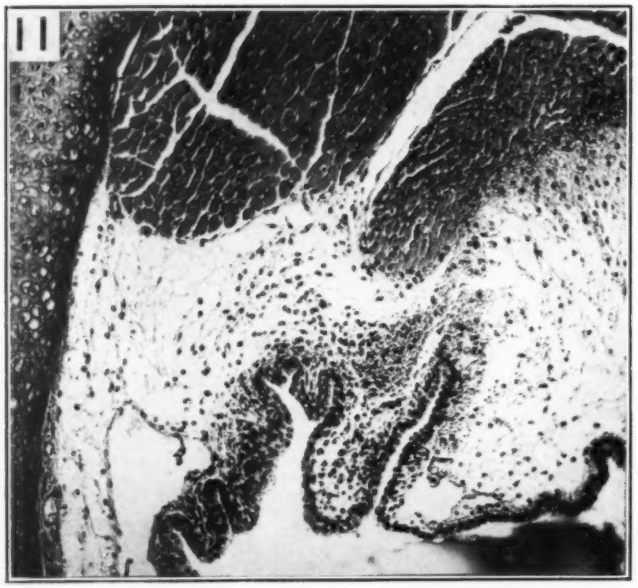


FIG. 7.—Section through a mesenteric artery of a desoxocortisone-treated rat: irregular hyalin deposits underneath dark line which corresponds to intima; endothelium is loosened and in some places intima is in direct contact with circulating blood; outer coats of this artery completely lost their normal structure because of proliferating granuloma tissue.

FIG. 8.—Periarteritis nodosa in a pancreatic vessel, with normal pancreatic acini on the left; similar changes were seen throughout pancreatic arterial tree; oedema and connective-tissue proliferation were evident even at a distance from vessels between the pancreatic acini.

FIG. 9.—Periarteritis nodosa and connective-tissue proliferation in submucosa of upper small intestine in a desoxocortisone-treated rat: note greatly dilated lymph vessel just underneath muscular coat.

FIG. 10.—Periarteritis nodosa and granulomatous proliferation of connective tissue in submucosa of stomach in a desoxocortisone-treated rat.

FIG. 11.—Intense oedema of stroma with marked dilatation of lymphatic vessels in glottis region of a desoxocortisone-treated rat.

afferent glomerular arterioles. Hyalin casts and great dilatation or collapse of tubules were also commonly observed (see Figs. 1 to 4, Special Plate).

The heart showed marked hypertrophy in the treated animals. This proved to be significant even in absolute terms, but the probability of the significance was even greater when expressed as a function of body surface. This enlargement was presumably the consequence of hypertension. It was accompanied by manifest signs of periarteritis nodosa of the cardiac vessels (see Figs. 5 and 6) and numerous islets of hyalinization underneath the endocardium. Many of these islets contained polynuclear giant cells similar to those seen in Aschoff's nodules.

The weight of the brain was likewise very significantly increased. This was quite obvious even at naked-eye inspection. As a result of brain oedema and increased accumulation of cerebrospinal fluid the still rather soft cranium of these young growing rats became distended and more rounded than that of the controls. At the same time the brain surface was extremely pale and moist owing to oedema. In all but one of these animals there also developed a characteristic encephalopathy, which we had previously noted in desoxycorticosterone-treated animals. It will be recalled that this is characterized by hyalinizing arteritis of the smaller brain vessels, often accompanied by small haemorrhages or the formation of foci of liquefaction necrosis. At the same time there is intense glial proliferation. The general histological characteristics of this lesion are highly reminiscent of those seen in man suffering from hypertensive encephalopathy, periarteritis nodosa of the brain, allergic encephalitis, the so-called "brain rheumatism," and other collagen diseases.

The mesenteric arteries of all our animals were affected by a diffuse and intense hyalinizing panarteritis such as is seen in very acute types of periarteritis nodosa in man. Throughout the mesentery the arteries were hardened and thickened as judged by examination on the necropsy table. Histologically, the most prominent changes were the deposition of homogeneous, hyalin, eosinophilic masses between the endothelium and the lamina intima. At many places the endothelium became loosened and thrombi had formed. In other locations the hyalin material appeared to infiltrate into the outer coats of the vessels. At the same time there was marked proliferation of a granulomatous tissue which led to the complete disorganization of the normal arterial-wall structure (see Fig. 7). In some instances these granulomas were studded with eosinophil leucocytes, but this latter change was not constant.

Essentially similar vascular changes were noted in the pancreas (see Fig. 8), the small intestine (see Fig. 9), the stomach (see Fig. 10), as well as throughout the skeletal musculature, etc. Everywhere intense connective-tissue proliferation accompanied the arteritis. In view of the frequent occurrence of gastro-intestinal connective-tissue proliferation in various collagen diseases (e.g., scleroderma) it is interesting to note that desoxocortisone, a natural adrenal steroid, can produce such changes under suitable experimental conditions.

Presumably as a consequence of the water and salt retaining effect of this mineralo-corticoid, oedema and marked dilatation of the lymph vessels are also very prominent in most organs. A particularly pronounced oedema occurred in the trachea, especially in the glottis region. The stroma of the tracheal mucosa was greatly swollen and the lymphatic spaces were conspicuously engorged (see Fig. 11). Since corticoids are known to be discharged in conditions of acute stress, such lesions may perhaps play a part in certain hitherto unexplained instances of acute oedema of the trachea and glottis.

Unlike the gluco-corticoids (for example, cortisone), desoxocortisone does not cause any significant involution of the lymphatic organs. Indeed the figures given in the table clearly indicate that the thymus underwent only an insignificant involution, while the iliac lymph nodes and spleen of the desoxocortisone-treated rats were actually (though not significantly) larger than those of the untreated controls. This agrees well with our previous observations, which revealed that, under comparable experimental conditions, desoxycorticosterone, unlike cortisone, causes no marked involution of the thymus and lymphatic organs (Selye, 1949a). The apparent enlargement of the lymph nodes is primarily due to a dilatation of the lymphatic sinusoids, as shown by our histological studies.

Neither the weight nor the histological structure of the adrenals showed any significant deviation from the normal after desoxocortisone treatment. It had previously been noted that, unlike cortisone, desoxycorticosterone causes only slight adrenal cortical involution, and it is a rather consistent characteristic of gluco-corticoids that they inhibit ACTH production by the pituitary, and hence cause "compensatory adrenocortical atrophy," more readily than the mineralo-corticoids. It is difficult to explain, however, why in the present series there was not even the slightest involution of the adrenal cortex. Perhaps the ability of desoxocortisone to inhibit ACTH production, by virtue of its specific pharmacological properties, is so slight that it was greatly overcompensated by the fact that it caused widespread organ damage; the resulting development of a general-adaptation syndrome would naturally tend to increase ACTH production.

The seminal vesicles of the desoxocortisone-treated (castrate) rats weighed 8.5 mg. (±0.5) as compared with 5.6 mg. (±0.7) in the controls. This slight enlargement was not accompanied by any histological signs of testoid activity and is probably merely the result of tissue oedema. It may therefore be concluded that desoxocortisone is not a virilizing compound; in this respect it again resembles desoxycorticosterone.

It is somewhat difficult to assess the relative toxicity of desoxocortisone in comparison with that of desoxycorticosterone, since we have not yet had occasion to examine the actions of the latter when administered in the form of such fine microcrystals (less than 10 μ). It may be said, however, that under no conditions has it been possible up to now to obtain such widespread hyalinosis with desoxycorticosterone within 24 days. Furthermore, such intense and widespread periarteritis nodosa as that which developed in the present experimental series has not yet been produced under any conditions with other steroid hormones. It may therefore be concluded that desoxocortisone is highly active in producing hypertension and the histological lesions of hyalinosis which are so characteristic of certain hypertensive, rheumatic, and allergic diseases of man.

Summary and Conclusions

Desoxocortisone (Reichstein's compound "S"), a steroid normally occurring in the adrenal cortex, proved to be highly active in raising the blood pressure and water turnover. It also caused widespread and intense periarteritis nodosa, acute nephrosclerosis, and granulomatous nodules in the heart, accompanied by organ changes similar to those which occur in certain so-called "collagen diseases" of man.

The data are interpreted as further evidence supporting the view that naturally occurring corticoids may be involved in the

pathogenesis of those "diseases of adaptation" which respond favourably to therapy with gluco-corticoids or ACTH.

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PROGRESS OF GASTRIC SURGERY IN THE LAST HALF-CENTURY*

BY

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I chose this subject for my address because I have had the rather unusual experience of having operated upon nearly 4,000 gastric lesions and because I have lived through practically the whole period of the growth of this surgical specialty. It was indeed an astonishment to me to find, when looking up the history for the first edition of my book, that the first gastro-enterostomy performed by Wolfer, the first excision of gastric ulcer by Rydygier, the first successful gastrectomy by Billroth, as well as the first cholecyst-enterostomy by von Winiwarter were all carried out in the year of my birth, and I felt that I had indeed been born under the upper abdominal star. Since 1900, when I first started as a medical student, I have seen great changes in the selection of cases for operation, in the methods of performing the operation, and in the choice of operation for the individual lesion.

I have been singularly fortunate in that I have worked under many of the pioneers of gastric surgery, as a dresser under Sir Frederick Eve, who was one of the earliest to perform many gastro-enterostomies. In his day, so serious an operation was this considered that he had all his hospital patients nursed in a separate room with day and night special nurses, and they were kept on rectal feeds with nothing whatever by mouth for two weeks. Later I served under Mr. Roxburghe, the ophthalmic surgeon, who performed the first partial gastrectomy in this country; and for a short time was house-surgeon to that brilliant young surgeon Mr. Harold Barnard, who even in his short life did so much to advance abdominal surgery. I was then appointed house-surgeon to Mr. Mansell-Moullin, who in his day was regarded as one of the greatest gastric surgeons in this country and who obtained very successful results, although he operated without gloves and while wearing three rings. Later I became registrar under those great abdominal surgeons Sir Hugh Rigby and Mr. James Sherren. To the latter especially I owe the greater part of my training, for not only was I his registrar at hospital but for several years was his private assistant, and after his retirement inherited from him the greater part of the upper abdominal surgery at the London Hospital.

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Changes in Custom

During my student days it was the custom to treat all cases of peptic ulcer medically and to call in the aid of the surgeon only in the case of some complication. It was my old chief, Dr. J. F. Smith, who introduced the powder which later became so popular as MacLean's powder, although, unfortunately for him, he did not advertise it. Many physicians even claimed that pyloric obstruction could be cured by repeated gastric lavage, a belief that died very hard, so that in my early days as a surgeon I had to treat many cases of carcinomatous obstruction which had become completely inoperable while undergoing prolonged courses of lavage, and with other surgeons had a great fight to establish the dictum that all cases of pyloric obstruction should be treated surgically, for the obstruction might be carcinomatous, and in any case was mechanical in nature and must be treated mechanically.

Even up to several years later many surgeons stated that they had never seen the characteristic pathological picture of duodenal ulcer which Lord Moynihan had described so graphically, and they denied its existence. Great controversy raged then, and has done so up to times within the memory of you all, whether severe haematemesis should be treated with complete rest, with a restricted diet, with a high protein diet, or by immediate operation. In the same period many if not most physicians were opposed to the surgical treatment of carcinoma of the stomach, for they believed that a cure could never be obtained and that it only subjected the patient to much discomfort in the remaining short period of his life.

About 1910 opinion had entirely changed and had reached the other extreme, the tendency being to advise operation as soon as a peptic ulcer was diagnosed, no attempt being made by the physician to carry out medical treatment or indeed to make a detailed investigation. In fact, at that period nearly all such cases were admitted to hospital direct to the surgeon and the full investigation was performed by him, so that the greater part of our modern knowledge of the symptomatology and means of diagnosis of peptic ulceration and carcinoma of the stomach is due to the surgeons. It is very regrettable that the modern student is being taught to pay so little attention to a carefully taken clinical history, which at that time was shown to be the most valuable method of investigation. There is no doubt, however, that in treatment the pendulum had swung much too far, and many cases that were unsuitable for surgery or that could have been cured medically were subjected to an operation, which in most cases was a gastro-enterostomy.

As a result a reaction set in, and, following the writings of MacLean, of Izod Bennett, and more especially of Sir Arthur Hurst, surgical treatment in the mid-1920's fell into a certain amount of disrepute. The last-named physician claimed that all cases of peptic ulcer could be cured with adequate medical treatment and that if not so cured the treatment was inadequate; nevertheless he

insisted that after the symptoms had disappeared the patient must conform to a most onerous life and a diet which was quite incompatible with a working man's life and which he called his post-ulcer regime. At about the same time there came into fashion the apparently unphysiological treatment of ulceration by duodenal intubation and by hypodermic medication, one form of which gained great popularity.

Indications for Surgery

It is indeed only in recent years that physicians and surgeons have reached a measure of agreement on the indications for surgery. For my own part it has long been my custom to teach that there is only one real indication for surgery in a case of peptic ulceration, and that is the failure of medical treatment. It may be said that this surely does not apply to obstruction and perforation, to which I reply that if medical treatment had been successful neither of these complications would have occurred. A warning must, however, be sounded: before starting medical treatment one must be certain that the case is not early carcinoma. This is frequently said to be a matter of great difficulty, but I firmly believe and have always taught that a carefully taken history, so often grossly neglected to-day, will always give at least a suspicion of carcinoma. This is specially so with severe haematemesis. It is still not uncommon to find that such cases are regarded, in spite of a very short history, as due to ulcer and are treated medically.

It is curious to note that the one condition which in the first decade of the century was regarded as an essential indication for operation—namely, perforation—has of late years been treated by Hermon Taylor and others with complete rest, constant aspiration of the stomach and duodenum, and intravenous fluid. Good results have been claimed, but from observations of the intraperitoneal conditions in many perforations I still feel that if I had a perforation myself I should demand operation by a skilled surgeon at the earliest opportunity.

Another most interesting change that has occurred in this country of recent years is in the nature of peptic ulceration itself. This aspect has been fully discussed by Sir Henry Tidy on several occasions. It is sufficient to say here that chronic ulceration is becoming more common in young people, that females are becoming more addicted to it, and that it shows a greater tendency to recur after operation. My own figures up to 1938 always showed an incidence of 2 to 3% of gastro-jejunal ulcers after gastro-enterostomy for duodenal ulceration, and it is interesting to note that although Mr. Sherren performed this operation as a routine, yet after I succeeded him at the London Hospital only two of his cases came to me with marginal ulceration. Since 1938 my own experience has been that its frequency is increasing. I still believe, however, that the modern young surgeons are going too far in their belief that every duodenal ulcer should be treated with partial gastrectomy.

It is universally agreed to-day that carcinoma of the stomach should be treated by early operation, which holds out the only hope of cure, and that the only contraindication is the manifest evidence of widespread secondary deposits.

Surgical Technique

In the operative technique there have been even greater changes. As most of you know, the earlier anastomoses were performed with that ingenious instrument Murphy's button. Probably very few of you have ever seen it, but there is no doubt that it was the first step in the development of end-to-end and lateral anastomosis. It has been discarded so long that I was astonished when I went to the United States in 1913 to find that the first three operations I saw in New York were gastro-enterostomies performed with the button; but it is only fair to state that the surgeon was not an American born, and when I told Charles Mayo about it he had some biting comments to make. Even in 1943 I operated upon a patient for a gastro-jejunal ulcer with a Murphy's button *in situ*, which had been inserted two years before in Italy. The button was soon afterwards replaced by decalcified bone plates and later by sutures. In the early days of suture the great fear of surgeons was leakage at the angles, a danger which disappeared with the change from interrupted to continuous sutures.

I wonder how many are conversant with the term "vicious-circle vomiting," yet an enormous amount of literature was once written upon it and many different forms of gastro-enterostomy were suggested as a means of preventing it. No loops, short loops, and long loops were advocated; some advised the opening should be isoperistaltic, others retroperistaltic; some that it should be close to the pylorus, and others that it should be remote from it; and many valvular openings were devised. Perhaps the most unsatisfactory methods were those in which a lateral union was made between the afferent and efferent loops, and the so-called Roux operation of an end-to-side anastomosis, for such methods were almost certain to be followed by gastro-jejunal ulceration. In fact, they are the very methods which to-day are used to produce experimental ulceration in animals. In 1912 Mayo showed that the vicious-circle vomiting was obstructive and due to constriction of the efferent loop by the mesocolon. He advocated that this structure should be sutured to the stomach and its edges turned in so as to reduce the possibility of scarring. Since then this complication has almost entirely ceased and the majority of young surgeons have never heard the term.

Gastro-enterostomy

Although to-day gastro-enterostomy has come to be regarded as a straightforward and easy operation there are certain technical points upon which I would lay great stress. As with all abdominal operations, the other viscera should first be examined. If the expected lesion be first sought for and found attention may become so fixed upon it that an examination of the other viscera is forgotten. I have met with cases in which a gastro-enterostomy has been performed for carcinoma of the colon, for congenital cystic dilatation of the bile duct, for cardiospasm, and even for gallstones.

The general law that no attention be paid to the pathology until the anatomy has been clearly demonstrated must be observed. This is especially so when the anatomy has been distorted by a previous operation. A further extension of this law is that no structure whatever should be divided until it and the surrounding structures have been clearly defined. The peptic ulcer must be visible and palpable, and when clearly demonstrated a decision must be made whether it is best treated by gastro-enterostomy.

Generally speaking, a posterior anastomosis is more satisfactory than an anterior one. The fold of the posterior wall which is clamped lies more easily if it is vertical, but its inclination is of little importance. The duodeno-jejunal flexure can be found lying on the left

of the second lumbar vertebra and the first loop of the jejunum drawn down. That it is this loop should be confirmed by drawing it down enough to see that its upper end is attached at the flexure. It would not seem possible that a mistake could arise in this respect, but I have had to operate upon two cases in which the stomach had been united to the lower ileum and upon one in which it had been joined to the transverse colon.

When identified a loop which lies in comfortable apposition with that of the stomach should be clamped. It should not be drawn down too tightly from the flexure to give a no-loop junction or be placed so far from it that small intestine can pass round it. It will generally be about 4 in. (10 cm.) from the flexure. The two loops are approximated with the afferent end of the jejunum at the upper end of the gastric loop if vertical or at the proximal end if it be oblique or transverse. Continuous sutures of chromic gut should be used and the inner layer should pass through all three coats, thereby firmly controlling haemorrhage. When the anastomosis is completed the mesocolon should be fixed to the stomach about ¼ in. (0.6 cm.) from the anastomosis with two or three catgut sutures.

Soon after Rydygier advocated wedge resection of a gastric ulcer it fell into disrepute, for in a considerable percentage of cases it was found to be followed by recurrences. This was rather to be expected, for if an ulcer could occur in a normal stomach how much more likely would it be to arise in a healing wound or operative scar? This drawback, however, seemed to be removed by combining the resection with a gastro-enterostomy, and for small indurated ulcers it became a very favourite operation. In the hands of different surgeons it was modified in several ways. Mayo excised the ulcer by the transgastric route, while Donald Balfour destroyed it with the cautery—a method which was very useful for ulcers high up.

It is my own practice to ligate the coronary artery on either side of the ulcer, to clamp the stomach right across by passing one blade through the gastro-colic omentum, up behind the stomach, and out through the gastro-hepatic omentum. This is done on either side of the ulcer; a wedge with its base at the lesser curve and containing the ulcer is excised, the posterior walls are first united with two layers of catgut suture, and then the anterior. The clamps having been removed, a posterior gastro-enterostomy is performed, running through the portion of stomach below the resection and lying parallel with the greater curvature.

Partial Gastrectomy

Of great interest has been the growth and development of the universally popular partial gastrectomy. The operation introduced by Billroth in 1881 consisted of removal of the affected pyloric portion of the stomach and the restoration of continuity by an end-to-end anastomosis, the duodenum being united to the lower end of the gastric opening, the upper end of which was closed. In the earlier cases there was a mortality of 64%, which was in large part due to leakage at the junction, for with interrupted sutures the closure of an angle is associated with considerable difficulty. Although in the earlier operations the amount removed was very inadequate, the method was based on sound physiological principles, and it was unfortunate that the failure to use continuous sutures so altered the course of the development of gastrectomy.

As a result of this danger Billroth introduced his second method whereby the openings of both the stomach and the duodenum were closed and a posterior gastro-enterostomy was performed to the proximal stump of the stomach. For many years this was the almost universal operation, and in 1910, when I was surgical registrar, the method was used by all the leading gastric surgeons. Later it was realized that in order to prevent recurrences in cases of carcinoma a larger portion of the stomach should be removed, and if this were done the stump of the stomach which was left was insufficient to allow a posterior gastro-enterostomy, or the making of such an opening in some cases endangered the vitality of the sutured edges of the stomach.

In 1910 my chief, James Sherren, evolved and performed the method of uniting the cut end of the stomach to the side of the jejunum. Unfortunately for British surgery, while he was collecting a sufficient number of cases for publication the method was independently published by Polya in 1911, and by his name the operation has since been known. It has been modified in the hands of many surgeons, but in some form or other is the operation usually performed to-day. In the original method a loop of jejunum was brought up through an opening in the mesocolon, and the afferent loop was united to the lesser curve of the stomach. Balfour brought the loop up in front of the colon but also joined the afferent loop to the lesser curvature, while Moynihan, also making it anticolic, united the afferent loop to the greater curve: others partly close the upper part of the gastric opening before making the junction.

For many years I performed the original Polya operation with satisfactory results, but was then persuaded by Lord Moynihan to try his method, as it was more rapid and avoided the opening in the mesocolon. At first I was very pleased with it and performed it in some 200 cases; but as my resections became larger, either because of higher-up ulcers or to get further, beyond the edge of a carcinomatous lesion, I found there was a tendency for the jejunum to kink at the upper end of the junction and to cause troublesome post-operative vomiting. I therefore abandoned it and returned to the original Polya operation.

Billroth's First Method

I had, however, always been enamoured of the first Billroth method, for I felt that the final condition was a much closer approximation to the normal stomach; but I had rather feared to perform it lest after removal of a large portion of the stomach there should be undue tension on the line of suture. It soon became evident, however, that the mobility of the greater curve is limited by a tight band which may be regarded as the left margin of the gastro-colic omentum or the lower portion of the gastro-splenic omentum; when this is divided the mobility is so greatly increased that it would be feasible to unite even the lower end of the oesophagus with the duodenum. There was the apparent paradox that the greater the amount of stomach that was removed the easier was the anastomosis. Since then I have used this method wherever possible, now performing it in nearly all cases, the chief exceptions being large adherent or scarred duodenal ulcers, and I have spent many a happy day in the operating theatre demonstrating the ease of its performance and the satisfactory technical result. I was much fortified in my choice, which was contrary to that of most surgeons, by finding that it was also the method preferred by that great master surgeon Professor Grey

Turner. It may be noted that the operation of Schoemaker, performed with his special clamp, is also a return to Billroth's first method, although in my opinion it does not remove enough of the greater curve.

On the many technical details which have made partial gastrectomy so successful and in the last 50 years have reduced the mortality from 50–60% to 1–2% I cannot enter here. It is sufficient to say that a large portion, in my opinion about seven-eighths, of the stomach should be removed so as to take away the greater portion of the acid-secreting area or to be as far beyond the edge of a growth as possible. In the general technique the biggest change has perhaps been that, with the introduction of the newer anaesthetics and careful pre-operative preparation, the danger of operative shock has almost disappeared, so that the time taken over the operation has become much less important. Nevertheless, when I see surgeons take three to four hours over a partial gastrectomy I feel that they have carried their leisurely methods too far. It should be the aim of a surgeon to perform no unnecessary actions, and the nearer he approaches this ideal the shorter time he will take. On the other hand, I would like to see every clock removed from the theatre and in its place inserted on the wall the short verse from the Book of Ecclesiastes, "Make no haste in time of trouble."

Even as late as 1930 total gastrectomy and removal of the cardiac end of the stomach by the abdominal, the abdomino-thoracic, or the pure thoracic approach were such rare operations that nearly every one was reported. In 1929 Finney and Reinhoff were able to collect only 67 reported cases. To-day they are being more and more frequently performed, some surgeons preferring one method of approach and others another. That so serious and extensive an operation for an otherwise fatal condition can give most satisfactory results in the hands of a skilled surgeon has been most ably demonstrated by Allison.

Choice of Operation

Of late years so universal has become the custom of treating all surgical lesions of the stomach and duodenum by a partial gastrectomy that any discussion on the choice of operation for an individual lesion may seem out of place. Nevertheless I cannot help but feel that this belief has gone too far and that to remove some seven-eighths of the stomach for an indurated simple ulcer of the lesser curve no larger than a sixpenny-piece is an unnecessary mutilation, although there is no question that it is one of the most satisfactory of all modern operations. One is, however, left in some doubt whether a sufficiently large number of cases have been followed up long enough and whether future experience may not reveal a large number of late complications.

Before, however, discussing the choice of operation for a given lesion I want to make it clear that in my opinion it is foolishness to state that there is only one operation for a given condition. Just as two mechanics or two carpenters may reach the same result by using different methods, each choosing that in which he is most skilled, so should a surgeon employ that method in which he is most experienced and which in his hands gives the best results, even if some other surgeon condemns it. The only acid test is a good follow-up department and a frequent analysis of end-results, which are compared with those of other surgeons. Therefore I can only give you my own decisions about the choice of operation and the results I have obtained thereby. Others may think they are bad and extol different methods, but I shall not quarrel with them.

What, then, is the choice of operation for a chronic duodenal ulcer? Whereas in the earlier days a gastro-enterostomy was always employed, to-day the majority of surgeons advocate a partial gastrectomy, because of their fear of subsequent gastro-jejunal ulceration. With a long history and marked pyloric obstruction there is usually a diminution of the free hydrochloric acid. For such cases many still advocate posterior gastro-enterostomy, which is my usual choice. Of course, if there is the slightest suggestion of pyloric carcinoma, which I believe is mainly evidenced by rapid onset of the obstruction, marked loss of appetite, and complete absence of free HCl, a partial gastrectomy should always be performed.

Is there, however, any place for gastro-enterostomy in simple cases of chronic duodenal ulcer? I believe there is; for my own figures, based upon most careful and complete follow-up observations, have shown a very constant incidence of gastro-jejunal ulcer of only 2%. It is my custom to combine the gastro-enterostomy with embedding of the ulcer with a running mattress silk suture—the so-called Kelling–Mayo suture—to limit the possibility of post-operative haemorrhage. Many cases that I have so treated have remained in perfect health, taking a full diet and performing full work, for 20 to 25 years. Nevertheless I am convinced that there are certain people who have a much greater tendency to develop gastro-jejunal ulceration, probably because they have a larger area of acid-secreting mucosa than normal. Such patients tend to develop duodenal ulcer symptoms early in life; the test meal shows a very high free acid. The radiograph reveals hypertrophy of the mucosal folds, and this is even more evident on gastroscopy.

With such patients it is always my custom to perform a partial gastrectomy. If the ulcer is small and mobile the duodenum is divided beyond it and a Billroth I operation performed. If it is large and adherent I would most emphatically protest against the modern tendency to free it from the pancreas and remove it entirely, a step which is often very prolonged and associated with an increased risk. It is always quite simple even to cut the ulcer across. With a double layer of catgut sutures the duodenum can always be closed and the end then embedded with a silk purse-string or mattress suture. In the blind end of the duodenum any ulcerated area will heal rapidly. A Polya type of gastro-enterostomy is then performed.

Much the same question will arise with a chronic gastric ulcer. Is there any place for the more local procedures, or should a partial gastrectomy always be performed? Many surgeons have told me that they find a wedge resection of an ulcer more difficult, tedious, and prolonged than a partial gastrectomy. If this is so and they are skilled in performing the latter operation, then there is no question that it should be the operation of their choice. I have, however, already stated that in my mind the removal of the greater part of the stomach for a small indurated ulcer in the middle of the lesser curvature seems an unnecessarily extensive procedure and that in my hands a wedge resection, followed by a gastro-enterostomy, has been a most successful operation, my follow-up department showing 92% of five-year cures. It should not, however, be performed for a large ulcer, as it may then cause considerable deformity of the stomach. In recent years, when surgical treatment has not been sought so early, the ulcers are usually larger and

the opportunities for resection have been fewer. In such cases a partial gastrectomy should be performed.

Carcinoma of the Stomach

The remaining indications for gastrectomy are, I think, clear. First and foremost, of course, is carcinoma of the stomach. It must be remembered that without operation this disease is inevitably fatal, for at present deep *x*-ray therapy holds out little if any hope. Every patient should therefore be given the chance, even if the hope of success appears to be a small one, the only real contraindication being the presence of definite metastases. The size of the tumour is no contraindication. Many years ago I described as a special type of carcinoma a very large tumour situated on the greater curvature in which glandular secondaries arise late and the tumour remains mobile.

This variety, which I have designated massive carcinoma of the greater curvature, arises, I believe, in an adenoma, and in spite of its size is usually easily removable. Apparent fixation of the tumour of course lessens the chance of removal, but some such cases turn out to be operable. If the growth be irremovable but associated with pyloric obstruction a gastro-enterostomy gives a very slight measure of relief. In 1914 W. J. Mayo advocated a partial gastrectomy in such cases, for he pointed out that even with multiple secondaries the relief that might be obtained was very considerable. With this view I am in entire accord. It must be remembered also that even if nothing can be done the patient's relatives will always feel that at least he was given a chance, and their minds will thereby be relieved.

One of the greatest improvements of recent years has been the steady increase in the percentage of operable cases. In 1906 Mr. Mansell Moullin used to say that the only hope of meeting a curable case was to get it before a tumour could be felt, and so far he had failed to do this. My own experience has been of interest: in my first five-year series 74.1% were inoperable, in the second 56.1%, but in the last only 40%. An interesting point in view of Mr. Mansell Moullin's remark is that a slightly higher percentage were operable with a palpable tumour than without. The percentage of cases free of recurrence for five years has also steadily risen until it is now 20 to 30%.

In performing the operation a very wide removal of the stomach must be carried out. It is usually called a subtotal gastrectomy, at least seven-eighths of the viscus being removed, but I am often astonished to see that many surgeons of repute perform a gastrectomy which in my opinion is far too small. It is also essential to remove the glands around the coeliac axis. For this purpose the stomach is turned over to the left, after the duodenum has been divided and the coronary artery ligated and divided as it arises from the coeliac axis, instead of in the left margin of the lesser omentum as is done with a chronic ulcer. It is my custom not to remove the great omentum as a routine, as was recommended by Hey Groves, but to reserve this step for those cases in which there is evidence of lymphatic infiltration of this structure. Whenever possible I restore continuity by end-to-end gastro-duodenostomy (Billroth I). In cases of leather-bottle stomach, wide infiltration, or carcinoma of the cardiac end a complete gastrectomy should be performed, the end of the oesophagus being implanted into the side of a loop of jejunum; but to-day all such cases will be diagnosed before operation and a decision made whether the approach should be abdominal, abdomino-thoracic, or thoracic.

Gastro-duodenal Ulcer

In my experience a gastro-jejunal ulcer ultimately requires operation. I have watched many cases which have had the benefit of long and careful medical treatment by the most skilled physicians, but they have always relapsed. It used to be the custom in such cases to excise the gastro-enterostomy and restore the normal relationships. Such an operation is useless, for it is always followed by a fresh duodenal ulcer. Nor is the local resection of the ulcer or the performance of a new anastomosis in Y, which has often been advocated, of any value, for the ulcer always recurs. The only satisfactory method is to perform an extensive partial gastrectomy, so that the acid-secreting area is much reduced.

The operation is often regarded as one of great difficulty, but if methodically performed it becomes relatively easy. The first essential is to free the mesocolon. With the colon turned up this is started from below, great care being taken to preserve the middle colic artery. The separation may sometimes be aided by dividing the gastrocolic omentum and working from above. When once the mesocolon is free the rest of the gastrocolic omentum is divided and the loop of jejunum can then be drawn up and the lesser omentum and duodenum divided in the usual way. The stomach and jejunal loop are clamped on either side of the anastomosis and divided, and since there is already a lateral opening in the jejunum it is wiser to perform the new anastomosis after the Polya method.

Conclusion

It is evident from the above summary that in the last half-century there has been enormous progress in gastric surgery, in the indications for operation, in the technique of the various operations, and in the choice of operation for the individual lesions. With this progress there have been almost unbelievable improvements in the immediate mortality and in the end-results, so that operations which in 1900 would have been regarded as impossible or so dangerous as to be unjustifiable are now easily and safely performed, and with their aid many cases of gastric carcinoma have been given hope of a permanent cure: but practically the whole progress has been in operative technique, and it almost seems that the great skill of this technique has reached its zenith.

The medical profession, however, cannot and will not remain satisfied with the present position, in which the cure of a diseased stomach lies in its removal. It is permissible to believe that, if medicine remains free from control and regimentation, fresh observation and research will lead to knowledge of the cause of these conditions, so that they will be prevented or cured at their very inception and in a relatively short time: perhaps in the lifetime of many of you these marvellously skilled operations will cease to be performed and will be regarded as curiosities of the past.

The Royal College of Nursing has issued some leaflets on agreements and standing orders relating to the conditions of service of nurses. It recommends that the principles embodied in them should be used by hospitals in a form most appropriate to the particular circumstances. They are obtainable from the General Secretary, the Royal College of Nursing, 1A, Henrietta Place, Cavendish Square, London, W.1, price 2s. 6d. the complete set. The leaflets for matrons, sister tutors, ward and departmental sisters, and staff and senior staff nurses may be bought separately.

ACUTE PERFORATED PEPTIC ULCER

A STUDY OF THE RECENT FALL IN MORTALITY

BY

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This paper records a study of 490 consecutive cases of acute perforation of peptic ulcer treated in this hospital from 1938 to 1948 inclusive, and discusses the factors which may have contributed to the considerable fall in mortality during that time.

Recent papers provide evidence that the mortality from acute perforation has declined from the high levels which prevailed before the war. DeBakey (1940) reviewed the literature published between 1930 and 1940, and his collected series of cases showed a total mortality of 25.2% in 16,752 cases and an operative mortality of 23.4% in 15,340 cases. Published series that allow a comparative analysis of the mortality in recent years show a uniform decrease in Great Britain, America, and Scandinavia (Table I).

TABLE I.—*Comparative Degrees of Mortality from Perforated Peptic Ulcer*

	Year	No. of Cases	Mortality
Illingworth, Scott, and Jamieson (1944) (Scotland)	1924	191	26%
	1943	376	14%
Sangster (1948) (Scotland) ..	–1939	100	24%
	1939–48	105	4%
McElhinney and Hozzer (1948) (America)	1935–7	72	31%
	1944–6	80	12%
Houston (1946) (England) ..	1939	199	13%
	1944	205	6%
Johansson (1947) (Scandinavia)	1930–4	62	24%
	1940–4	69	12%

In addition, recent publications provide a number of series with low mortalities. Baritell (1947) had only three deaths among 90 admissions, and two of these occurred in patients who were not operated on. McClure (1940) had a mortality of 7.7% among 91 cases, and Graham and Tovee (1945) recorded 8.8% among 114 admissions, with only 6.3% in the operated group.

These figures provide evidence of a trend, but further analyses are needed, because there are many factors which affect the interpretation of fatality rates. The age distribution of the groups, the time interval between perforation and operation, the comparison of personal series with mass hospital figures, and the natural bias in favour of publishing successful rather than unsuccessful series provide some of the statistical pitfalls in comparing groups. To obtain the clearest assessment of the factors responsible for a fall in mortality it is desirable to study the problem in one unit over a number of years.

Present Investigation

Our series—consisting of 455 patients with frank acute perforation who received surgical treatment and 35 patients who for various reasons were not operated on—was treated between 1938 and 1948. During this period there were also 20 non-fatal admissions for "leaking ulcer." These last are patients on whom operation was not performed because it was felt that the perforation had sealed off : in many of them the diagnosis was not firmly established and the group has been excluded, as is usually done in other published series of acute perforation.

Ulcers clearly within the pyloric antrum have been classified as gastric, but the juxtapyloric ulcers have been included in the duodenal group, as recommended by Illingworth, Scott, and Jamieson (1944). Cases subsequently found to be carcinomatous have been included if their initial operative diagnosis was simple gastric ulcer ; these are the subject of a paper by Dr. R. Doll at page 215 of this issue.

In this series the greatest care has been taken to ensure the inclusion of all patients, not omitting those who died soon after admission and those whose perforation had been diagnosed only at necropsy.

The age and site distribution is shown in Table II. Comparison with other series reveals important differences,

TABLE II.—*Series 1938–48. Age and Site Distribution*

Age (Years)	Total	Deaths	G.U.		D.U.		J.U.		?	
			M	F	M	F	M	F	M	F
15–	3	—	—	—	3	—	—	—	—	—
20–	14	—	3	1	9	1	—	—	—	—
25–	34	2	2	—	30 (2)	2	—	—	—	—
30–	47	4	11 (2)	2	32 (2)	1	1	—	—	—
35–	53	3	4 (1)	1	43 (2)	2	3	—	—	—
40–	62	4	10 (1)	—	47 (1)	4 (1)	—	1 (1)	—	—
45–	57	10	13 (7)	2	39 (2)	3 (1)	—	—	—	—
50–	50	10	4 (2)	2 (1)	42 (7)	1	1	—	—	—
55–	59	15	14 (5)	1	39 (9)	3 (1)	2	—	—	—
60–	44	17	18 (7)	4 (3)	22 (7)	—	—	—	—	—
65–	34	9	6 (1)	3 (1)	21 (4)	3 (2)	—	—	1 (1)	—
70–	18	11	7 (3)	2 (1)	7 (6)	2 (1)	—	—	—	—
75–	10	7	2 (2)	2 (2)	5 (3)	1	—	—	—	—
80–	3	2	2 (1)	1 (1)	—	—	—	—	—	—
85+	2	2	—	—	2 (2)	—	—	—	—	—
Total	490	96	96 (32)	21 (9)	341 (47)	23 (6)	7	1 (1)	1 (1)	—

M : F = 9·9 : 1. D.U. : G.U. = 3·1 : 1. The numbers of deaths are shown in parentheses.

which are being studied further. We are here concerned with the change in mortality that has occurred during the period 1938 to 1948 inclusive. The mortality has fallen very appreciably during that 11-year period (Table III).

TABLE III.—*Mortality in the Series*

	1938	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948
Total cases	39	36	32	40	35	47	48	45	53	58	57
Total deaths	12	9	7	9	13	6	10	9	10	8	3
Unoperated cases											
Number	—	1	—	2	2	3	7	4	7	6	3
Deaths	—	1	—	2	2	3	6	4	7	5	2
Operated cases											
Number	39	35	32	38	33	44	41	41	46	52	54
Deaths	12	8	7	7	11	3	4	5	3	3	1

This would be expected if the population concerned had become younger, if the time interval between perforation and operation had been reduced, if the number of non-operated late cases had declined, or if the technique of operation or aftercare had improved.

The improvement has been effected in spite of an older population being admitted, without an appreciable fall in the proportion of late cases, and notwithstanding the admission of a higher proportion of moribund cases in which the diagnosis was not established. It follows that the improvement must be due to a better routine associated with operation and aftercare. To demonstrate these points the first three years have been compared with the last two

*In receipt of an expenses grant from the Medical Research Council.

TABLE IV.—*Comparison of Early and Late Years of the Period*

	1938–40	1947–8
Total No.	107	115
No. not operated	1 (1 died)	9 (7 died)
Total deaths	28	11
Total operative deaths	27	4
No. of cases over 70	3	9
No. of cases perforated:		
Not more than 12 hours before operation (or admission if not operated)	83	92
24 hours or over	5	4

years (Table IV). These periods provide approximately equal total figures and represent two periods, before and after the introduction of antibiotics and of modern anaesthetic techniques.

The increase in the number of cases not operated on in the later years is mainly due to three factors. First, more unsuspected perforations have come to light because for all deaths in hospital within 24 hours of admission a coroner's post-mortem examination is now performed, whereas previously a death certificate might have been issued without a post-mortem examination, and this was most likely to happen with the elderly. For example, the man aged 80 who was recently admitted with a six-months history of anginal pain and sudden onset of severe precordial and upper abdominal pain would probably have been certified as dying from coronary thrombosis and the unsuspected acute perforation would have remained unrecorded. Secondly, since 1940, necropsies have been performed on 64 out of 68 dying from bleeding peptic ulcer, and the diagnosis of associated perforation was confirmed in six of them. It is unlikely that as high a proportion were previously subjected to necropsy or that the same proportion is true for other hospitals. Thirdly, the proportion of admissions over 70 years of age has increased, and it is these elderly folk, often living alone without friends or relatives near by—so often the case in large cities—who come in moribund, having perforated often more than 24 hours previously, some indeed having been completely prostrated by the perforation and having been unable to attract assistance for long periods.

Non-operated Cases

During the period of this series there has been no change in surgical policy towards the late cases. The increase in non-operated cases is essentially due to the greater accuracy of diagnosis, to the insistence on post-mortem examinations, and to the much larger number of very elderly admissions; the matter, however, needs further consideration.

In the whole series there were 35 patients on whom no operation was performed; of these, 32 died. They fall into three categories.

In the first there were 13 patients who were admitted with gross peripheral circulatory failure; all of them died within a few hours. Their history suggested that perforation had occurred at least 12 hours previously and mainly between 24 and 72 hours before admission. Eight of the 13 were over 65; the youngest was 58.

The second group comprised nine patients for whom operation was not advised or (in one case) was refused by the patient; three recovered. Three in this group were really suitable for operation, but it was decided to follow the technique of medical treatment advocated by Hermon Taylor (1946); two of the three died. The remaining six were treated medically because operation was refused or because of very serious associated medical conditions—e.g., gangrene of leg, an extreme degree of emphysema, or senility.

In the third group (13 patients) the diagnosis of acute perforation was not made during life, although it may have been considered as a possibility. It is noteworthy that in six of these patients, aged 47, 59, 73, 76, 78, and 79 years, there had been very severe gastro-duodenal bleeding and they were profoundly ill but showed none of the usual manifestations of acute perforation, although one was thought to have had a pulmonary embolism. In the other seven cases there was little to suggest the diagnosis. One was already moribund with Hodgkin's disease, two were unconscious on admission, and the others were *in extremis*— ? coronary infarction. One was admitted with a subphrenic abscess, shown at necropsy to be due to a perforated ulcer.

Operated Cases

The fall in mortality among the operated cases treated in hospital has been particularly impressive. Table IV shows that during 1938–40 there were 106 cases, with 27 deaths. In 1947–8 there were the same number, with only four deaths.

The fall cannot be explained by a change in the age distribution of the population. There has been a slight increase in the number operated on within 12 hours of perforation (Table V), but not sufficient to contribute materially to the improved results. The improvement has been seen in all age groups (Table VI) and in both early and late cases, but has affected duodenal more than gastric ulcers (Table VII).

TABLE V.—*Comparative Mortality by Delay Before Operation*

	1938–40		1947–8	
	No.	Deaths	No.	Deaths
Up to 12 hours	83	16 (19·3%)	90	4 (4·4%)
Over 12 ,,	22	11 (50%)	14	0
?	1	—	2	—

TABLE VI.—*Comparative Mortality by Age*

Age	1938–40		1947–8	
	No.	Deaths	No.	Deaths
Up to 35 years	27	4	27	0
35–69 ,,	76	22	75	3
70+ ,,	3	1	4	1

TABLE VII.—*Comparative Mortality by Site*

	1938–40		1947–8	
	No.	Deaths	No.	Deaths
Gastric	23	7	24	2
Duodenal	83	20	82	2
Jejunal	—	—	—	—
Total	106	27	106	4

The improvement is reflected in the change in the causes of death and in the frequency of complications.

Before 1943 there was a high proportion of early deaths from post-operative shock or from general peritonitis, the patients dying within two days. Since 1943 there have been no early deaths, and the delayed deaths have been associated with haemorrhage, subphrenic abscess, or various miscellaneous complications. The change of character

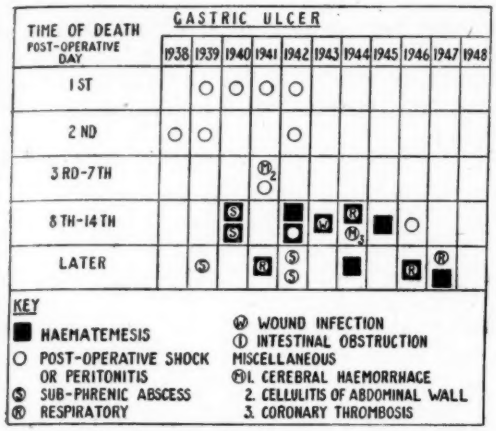

CHART 1.—Acute perforations. Operated cases of gastric ulcer, 1938–48. Cause and time of death.

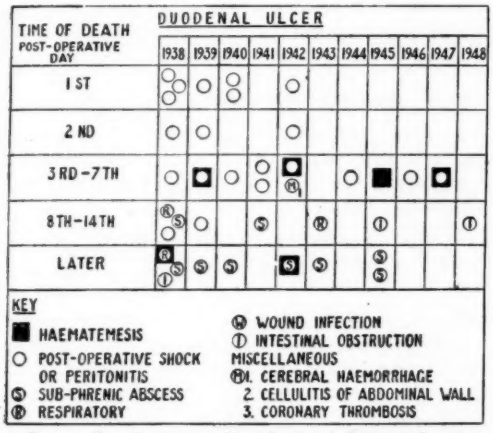

CHART 2.—Acute perforations. Operated cases of duodenal ulcer, 1938–48. Cause and time of death.

and time of death are shown well in Charts 1 and 2, which also bring out the importance of associated haemorrhage as a factor contributing to the fatality.

The incidence of and mortality from major complications are shown in Table VIII. It will be noted that the incidence of respiratory complications has remained constant but that the associated mortality has greatly declined. It will also be noted that during the past two years lung abscess and empyema have disappeared and the frequency of both subphrenic abscess and wound infection has fallen considerably. Possible factors contributing towards this fall in mortality include improved surgical technique, improved anaesthesia, the routine use of antibiotics, and better post-operative care.

TABLE VIII.—*Complications*

	1938–40		1947–8	
No. of admissions	106		106	
Deaths	27		4	
Complications	No.	Deaths	No.	Deaths
Post-operative shock or peritonitis	16	14	1	0
Chest:				
Basal collapse, pneumonitis, bronchitis	40	7	44	2
Lung abscess	3	2	0	0
Empyema	2	2	0	0
Subphrenic abscess	8	7	1	0
Wound infection	36	6	10	2
Haematemesis/melaena	10	4	7	2

The series has not been correlated with the seniority of the surgeons concerned, but this could offer no explanation of the improvement in recent years. During the pre-war and war years the cases were invariably operated on by a resident senior surgeon, but since the war many more have been operated on by surgical assistants.

During the period reviewed there have been important changes in anaesthetic technique, notably the introduction of cyclopropane and curare. In the earlier years most patients were anaesthetized with gas, oxygen, and ether, and a deep anaesthetic was necessary to overcome the rigidity of the abdominal muscles; the use of cyclopropane allowed a much lower concentration of ether. The introduction of cyclopropane coincided with the increased use of sulphonamides, and curare and penicillin came into general use almost simultaneously.

TABLE IX.—*Acute Perforations. Operated Cases*

	1938	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948
Total No.	39	35	32	38	33	44	41	41	46	52	54
Deaths	12	8	7	7	11	3	4	5	3	3	1
Sulphonamides	—	2	6	10	19	41	41	38	42	50	52
Cyclopropane	—	—	—	—	6	22	35	38	39	49	54
Penicillin	—	—	—	—	—	—	—	5	8	47	54
Curare	—	—	—	—	—	—	—	4	12	46	50

Table IX shows the different factors which may have influenced the fall in mortality, and their time of introduction.

Discussion

These results clearly demonstrate a remarkable fall in the mortality from acute perforation of peptic ulcer. In the first 106 operated cases (1938–40) there were 27 deaths; in the last 106 (1947–8) there were only four. The series was not arranged as a statistical study of new anaesthetics or antibiotics, and new methods were introduced as they became available. Table X shows the progressive and

TABLE X.—*Effects of Antibiotics and Anaesthetics (Excluding Local and Spinal)*

Sulphonamides	–	+	+	+
Cyclopropane	–	–	+	+
Penicillin	–	–	–	+
Curare	–	–	–	+
No. of cases	139	66	109	92
Deaths	31	10	12	4
Mortality	22·3%	15·2%	11·0%	4·3%

significant fall in mortality with the use first of sulphonamides, then of cyclopropane, and, finally, of penicillin and curare. Unfortunately, the total numbers are not large enough to determine whether the reduction was significant at each stage, but there is no doubt about the significant fall over the whole period.

It is probable that the antibiotics have played a larger part than the new anaesthetic techniques, for subphrenic abscess and purulent chest and wound infections have all shown a substantial decline in frequency and mortality. Better anaesthesia may well have contributed to the disappearance of the early deaths after perforation, as the toxic effects of heavy anaesthesia can now be avoided. The better relaxation achieved means less trauma to peritoneal structures, and this may reduce the frequency of abdominal complications. However, antibiotics have certainly cut short the post-operative peritonitis which formerly took its toll of early deaths.

Two further points suggesting the superior role of antibiotics are that spinal analgesia did not appreciably lower the operative mortality before the introduction of chemotherapy, and that at Hillingdon Hospital, a hospital similar to the Central Middlesex, during the past three years there have been 16 deaths among 116 operated cases. Curare was used extensively, but penicillin and sulphonamides were not given as a routine. The corresponding figures at this hospital, where there was a routine use of antibiotics, are seven deaths in 152 cases. To establish firmly the

relative parts played by antibiotics and better anaesthesia would probably need a survey of cases from many hospitals, but the point is mainly academic.

An acute perforation is a major crisis for the body, and it is entirely reasonable to bring the best possible help to counter infection; routine penicillin and sulphonamides provide complementary assistance against Gram-positive and Gram-negative bacteria. It is noteworthy that the mortality has declined most in the duodenal ulcer group (Table XI). The early deaths have disappeared from both

TABLE XI

	Gastric		Duodenal	
	1938–42	1943–8	1938–42	1943–8
Total No.	47	53	129	219
Deaths within first week	9	0 (10)	17	4 (29)
Later deaths	8	9 (9)	11	6 (19)

Expected deaths in parentheses, calculated on 1938–42 rate.

the gastric and the duodenal ulcer groups, but, although the deaths after the first week have greatly diminished in the latter, there is no corresponding fall in late deaths from gastric ulcer.

It is clear from the charts that associated haemorrhage has contributed particularly to this high delayed mortality and raises the advisability of emergency partial gastrectomy in selected cases of acute perforated chronic gastric ulcer. The problems of associated haemorrhage and perforation are being considered in a further paper.

The particular interest in post-operative care, apart from the use of antibiotics, has probably increased the comfort of the patient rather than had any real effect on the mortality. The administration of adequate amounts of fluids, avoiding any excess of salt, prevents the discomfort of dehydration and the dangers of hydraemia. Particular attention to the chest and stimulation of coughing and expectoration probably reduce the incidence of massive collapse of the lungs.

It may be thought that the fall in operative mortality must to some extent be due to the higher proportion of non-operated cases in the later years. If this were associated with a change in attitude by the surgeon towards the desperately ill it would indeed be an important factor. However, as previously stated, this is not so, and the increase of non-operated cases is due to improved diagnosis in the moribund group and to an increase in admissions among the oldest age groups.

Except in three extremely ill and complicated cases, no attempt has been made to assess the value of the medical management of acute perforation, but the present figures suggest that emergency operation, and therefore the elimination of faulty diagnoses, will remain the treatment of choice. Hermon Taylor (1946) reported 28 cases treated conservatively, with four deaths; and Visick (1946) had 14 cases, with three deaths. The combined series is small, but the results do not suggest that conservative treatment will equal modern surgical practice.

It should be pointed out, however, that Hermon Taylor did not give sulphonamides or penicillin, and that Visick used only sulphonamides. Perhaps the full assessment of medical management must await an unselected series in which full use is made of modern antibiotics. Medical management will certainly always play its part in those cases in which operation is virtually excluded by the severity of associated complications and in those which perforate when surgical assistance is unobtainable.

In previous series the increase in mortality with the increase in length of time between perforation and operation has often been recorded. It was noted in this series that this was true only for duodenal ulcer (Table XII).

TABLE XII.—*Showing Lapse of Time Between Perforation and Operation*

	Hours:	0–3	3–6	6–12	12–18	18–24	Over 24
Gastric ulcer	No. ..	9	37	33	11	7	2
	Deaths ..	6	8	7	2	2	1
	Mortality %	66·7	21·6	21·2	18·2	28·6	50
Duodenal ulcer	No. ..	48	160	91	19	13	13
	Deaths ..	2	8	9	6	6	7
	Mortality %	4·2	5·0	9·9	31·6	46·1	53·8

It is probable that acute perforations account for between 40 and 50% of the deaths from peptic ulcer, which in England and Wales are of the order of 5,000 a year. Halving the mortality from acute perforation would represent a reduction of at least a thousand deaths a year. Inquiry has shown that in some hospitals antibiotics are not given as a routine after operation.

Management of Cases

During the war years one of the three senior surgeons was always resident, and since the war an experienced senior assistant has been on duty within the hospital. A senior anaesthetist has always been quickly available. From 1940 practically all cases have been seen by one of us (F. A. J.), and the majority have been sent from the theatre to the medical dietetic wards, where the responsibility for post-operative care has been undertaken by the medical firm. On return from the theatre the patients are placed in a semi-reclining position but without knee pillows.

The fluid intake has been maintained at a minimum of 6 pints (3.4 litres) daily by giving continuous rectal fluid, using a rubber catheter (size 12 Jacques) connected by tubing with a drip connector and screw clip to a douche-can. Patients are very rarely intolerant of rectal administration of fluids given in this way, and with most there is no discomfort. It is an extremely simple and satisfactory technique. The accompanying schedule is used.

	24-hour Periods			
	1st	2nd	3rd	4th
By mouth ..	1 oz. (28 ml.) hourly	3 oz. (85 ml.) hourly	5 oz. (140 ml.) 2-hourly	Light diet 2-hourly
Per rectum ..	6 pints (3·4 litres)	4 pints (2·3 litres)	3 pints (1·7 litres)	—

Dilute saline was given (one part normal saline to four parts of tap-water). This avoids an excess of salt, which causes hydraemia and oedema. If, however, there is post-operative vomiting or if gastric fluid is removed by aspiration the equivalent volume of normal saline is given intravenously to cover the lost fluid. This enables the electrolyte balance to be preserved and any gross excess of sodium chloride is avoided. A Ryle's tube is kept in the stomach for the first 24 hours, and longer if there should be any accumulation of gastric contents.

Penicillin, 200,000 units, is given pre-operatively and 100,000 units six-hourly intramuscularly for three days. Sulphadimidine is given by mouth as crushed tablets, 4 g. on return to the ward and 2 g. six-hourly for three days.

Particular attention has been paid to the chest, and the ward sister has made it her responsibility to ensure deep breathing and the coughing-up of sputum at four-hourly

intervals throughout the day; the patient is also encouraged by firm pressure on the chest. If pain is too severe a preliminary injection of pethidine, 100 mg., is given.

Should there be any evidence of circulatory failure a rapid transfusion of intravenous saline is given, with, if necessary, plasma. Apart from cases with associated haemorrhage, it has rarely been necessary to transfuse with blood.

At operation, simple suture has been undertaken and usually omentum is brought over the ulcer. Particular care is taken to swab above the liver for residual fluid.

Post-operative pain is alleviated by morphine 1/6 gr. (11 mg.) at night, and pethidine, 100 mg., intramuscularly by day, for the first two or three days. An enema is given on the third morning. The patient is allowed up on the fourth day and the sutures are removed on the tenth day. If any evidence of venous thrombosis is discovered anticoagulant therapy as described by Ball and Hughes (1949) is started.

Summary

An analysis is presented of 490 cases of acute perforation treated from 1938 to 1948, inclusive.

The total mortality and the operative mortality have fallen considerably.

During the first three years the operative mortality was 27%; during the last two years it was only 4%. It was thought that this improvement is mainly due to better anaesthesia and to the routine use of antibiotics.

A summary of routine management of cases is presented.

We wish to express our thanks to the surgeons who have allowed us to treat these cases post-operatively: Mr. T. G. I. James, Mr. J. D. Fergusson, Mr. N. M. Matheson, Mr. J. Bonnin, and Mr. C. Chapple. We are also most grateful to the anaesthetists, Dr. Rankin, Dr. Davenport Jones, Miss McClelland, and Miss Ransom, and to the ward sisters who have given us such great assistance; we should like to mention particularly Sister Edmunds and Sister Johnstone. We wish to thank Mr. Duncan, of Hillingdon Hospital, who kindly supplied the figures from his hospital, and to Mr. J. Wilson for help in tracing the earlier cases.

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A study of the arrangements for the care of children under school age is being made by Miss Gladys Pendred, Federal Officer of the Australian Association for Pre-school Child Development, during a two months' visit to the United Kingdom under the auspices of the British Council. Her programme includes visits to nursery schools, organizations dealing with research and guidance, teachers' training colleges, and central and local government departments. She arrived in Britain on January 7 and spent the first three weeks in London. Later she will probably visit Scotland for two weeks and Durham for a few days. Trained as a teacher, Miss Pendred became Director of Free Kindergartens in Melbourne in 1925, was Principal of the Kindergarten Training College, Perth, from 1928 to 1937, and Supervisor of the Kindergarten Union of Western Australia from 1940 to 1941.

PERFORATED CARCINOMA OF THE STOMACH SIMULATING PERFORATED GASTRIC ULCER

BY

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Occasional instances of perforation complicating carcinoma of the stomach have been reported for many years, but only recently has the condition been recognized to be common. Aird (1935) could find only 71 cases in the literature, to which he added seven cases from the records of the Edinburgh Royal Infirmary and one personal case. Since then several large series have been reported, including 36 by Boyce (1946), 44 by Bocharov (1944), and 133 by McNealy and Hedin (1938).

According to Bisgard and Overmiller (1944), perforation occurs in from 3 to 6% of all cases of gastric carcinoma admitted to hospital, the average incidence being 4%. In about half the cases the signs and symptoms are obscure and many have not been recognized until after death. The other half clinically resemble perforated peptic ulcers and are of particular interest, as they are often early cases and eminently suitable for radical surgery.

At the Central Middlesex Hospital, in the eleven years 1938–48, there have been 17 instances of perforated carcinoma of the stomach. Perforations were found at operation 11 times, but only three were recognized to be carcinomatous. A fourth was diagnosed as carcinoma by gastroscopy shortly afterwards, but seven were discharged from hospital with the diagnosis of simple gastric ulcer. Contrary to belief, perforation in a carcinoma does not result in the early development of peritoneal secondaries, and failure to make the diagnosis must be considered particularly unfortunate, as it is likely to occur when the lesion is local and when resection may offer a reasonable prognosis. The object of this paper is to draw attention to the frequency with which perforation occurs in carcinoma of the stomach and to suggest how the risk of misdiagnosis may be reduced.

Brief details of the 17 cases are shown in Table I. Fuller histories of the misdiagnosed cases are appended.

In some of the first seven cases it can be argued that the lesion was a simple ulcer at the time of perforation and that carcinoma developed subsequently in the ulcer or independently elsewhere in the stomach. The latter would seem unlikely because of the close relation between the site of the perforation and of the carcinoma when diagnosed. The former is a possibility in Cases 4, 5, and 6, in which the intervals between perforation and definite evidence of a neoplasm were 26, 30, and 22 months respectively, but in the others the intervals were short, being in each case less than one year. Two and a half years, however, is not a long history for carcinoma of the stomach, and it is more reasonable to believe that the perforation was related to the carcinoma in all.

During the same period, 1938–48, a total of 452 patients with perforation of the stomach and duodenum were operated on, 449* of which were thought to be benign

*The 455 perforations operated on, reported by Avery Jones, Parsons, and White (1950), included seven cases of jejunal ulcers and excluded Case 8 above, which was recognized to be carcinomatous before discharge from hospital.

TABLE I.—*Cases of Perforated Carcinoma of Stomach*

No.	Sex	Age	Findings at Operation for Perforation	Result
1	M	42	Perforated P.U. on anterior wall near greater curve 5 in. (12·7 cm.) from pylorus	Further operation 10 months later. Inoperable carcinoma anterior wall and greater curve; secondaries in liver
2	M	62	Perforated P.U. in antrum	P.M. 4 months later. Carcinoma of lesser curve and antrum
3	M	56	Perforated ulcer in antrum; ? P.U., ? carcinoma. Discharged hospital as P.U (See case report)	P.M. 4 months later. Carcinoma, pyloric region of stomach; secondaries in peritoneum
4	M	49	Perforated P.U. on lesser curve 2 in. (5 cm.) above pylorus	Further operation 26 months later. Carcinoma of lesser curve; partial gastrectomy
5	M	34	Perforated P.U. high on anterior wall	Barium meal 30 months later. Neoplasm of cardia. Further operation 39 months after perforation. Carcinoma of cardia; partial gastrectomy
6	M	73	Perforated P.U. high on anterior wall near lesser curve	Barium meal 22 months later. Extensive neoplasm of fundus. P.M. 24 months after perforation: leather-bottle stomach
7	M	49	Perforated P.U. on middle of lesser curve	P.M. 5 months later. Carcinoma of pylorus extending up to middle of body
8	M	64	Perforated P.U. at pylorus	Further operation 4 months later. Inoperable carcinoma, pyloric region
9	F	75	Perforated carcinoma at fundus, inoperable	Died 3 days later. P.M. refused
10	F	72	Perforated carcinoma of pylorus, inoperable	Further operation 3 weeks later. Inoperable carcinoma of antrum Died 5 years later
11	F	71	Perforated carcinoma near cardia, inoperable	Barium meal 3 weeks later. Extensive carcinoma of body
12	M	60	No operation, patient moribund	P.M.: perforated carcinoma of lesser curve, 2½ in. (6·35 cm.) from pylorus
13	F	34	Operation abandoned, patient too ill	P.M.: perforated carcinomatous ulcer of stomach (site not recorded)
14	M	75	No operation (known carcinoma of stomach)	P.M.: carcinoma of antrum. Perforated in 2 places
15	M	70	No operation (diagnosed perirenal abscess)	P.M.: carcinoma high on lesser curve, perforated into lesser sac
16	M	69	No operation (diagnosed ? ruptured bladder)	P.M.: perforated carcinoma of stomach (site not recorded)
17	M	42	No operation (diagnosed pulmonary tuberculosis)	P.M.: pulmonary tuberculosis; perforated carcinoma middle of lesser curve of stomach

at the time of operation. These have been analysed by sex, age, and site (Tables II and III) to determine whether the cases which were finally diagnosed as carcinoma had any special characteristics which might have helped to differentiate them from the benign ulcers.

As was to be expected, there were relatively fewer carcinomas in patients under the age of 40, and none were observed in those under 30. The total number of cases is, however, too small to make it certain that carcinoma can be excluded at any age.

The total number of female perforations is also too small for it to be concluded that the risk of carcinoma attached to perforation in women is different from that in men. On the other hand, the annual number of deaths from carcinoma of the stomach is practically the same in both sexes, so that carcinomatous perforations might be expected to occur with equal frequency in both sexes. The fact that all the perforations which were mistaken for simple ulcers occurred in men suggests that there is possibly some factor which makes men particularly liable to this complication.†

TABLE II.—*Sex and Age Distribution of Patients with Perforations of Stomach and Duodenum Considered Benign at Operation*

Age	Male		Female	
	Final Diagnosis		Final Diagnosis	
	Benign	Malignant	Benign	Malignant
Under 30 ..	47	0	4	0
30— ..	88	1	6	0
40— ..	103	3	9	0
50— ..	94	1	6	0
60— ..	60	2	5	0
70+ ..	14	1	5	0
All ages ..	406	8	35	0

In Table III the male cases have been analysed by site. It is seen that all the duodenal perforations, as was to be expected, proved to be benign. Ulcers described as pyloric or juxtapyloric at operation are, in modern practice, generally classified with duodenal ulcers, and barium meals subsequently showed their duodenal site in several of the patients. However, exact location at operation is difficult, and the possibility of pyloric ulcers being gastric must be remembered. One such case was certainly observed as one proved to be a carcinoma.

TABLE III.—*Site Distribution of Males with Perforations of Stomach and Duodenum Considered Benign at Operation*

Site	Final Diagnosis	
	Benign	Malignant
Duodenum	283	0
Pylorus	44	1
Stomach	79	7
Antrum	23	2
Lesser curve (middle) ..	30	2
Lesser curve (upper third) ..	14	1
Anterior wall	11	1
Greater curve	1	1
All sites	406	8

Subdividing the gastric ulcers according to site, it is seen that misdiagnoses were made in all parts of the stomach. It is generally recognized that ulcers on the greater curve and in the antrum are particularly likely to be malignant, and this series provides no exception, though it is too small for independent conclusions to be drawn. While, therefore, the general risk of an apparently simple perforated ulcer being malignant was low (8 in 449—i.e., 1.8%), it was appreciable in the limited group of male gastric ulcers (7 in 86—i.e., 8.1%). As no attempt was made to trace the patients who did not return to the hospital, the risk may have been even greater.

Histories of the Misdiagnosed Cases

Case 1.—A man aged 42 was admitted on September 8, 1941. with ten years' history of intermittent epigastric pain two and a half hours after meals, worse one week ; severe pain for one day. At operation a large chronic ulcer was found on the anterior wall near the greater curve of the stomach 5 in. (12.7 cm.) from the pylorus, containing a perforation ¼ in. (0.3 cm.) in diameter ; the perforation was sutured. A test meal on September 18 showed no free acid, and gastroscopy on the 26th revealed considerable puckering of the folds where the ulcer had been sutured, but no ulcer was visible. He was readmitted on July 25, 1942, with a recurrence of pain for four months, and a big mass was palpable in the epigastrium. Barium meal and gastroscopy confirmed the presence of a carcinoma on the anterior wall and greater curve, and at operation a large inoperable mass was seen in the stomach, with secondaries in the liver.

Case 2.—A man aged 62 was admitted on May 3, 1942, with a history of intermittent epigastric pain and flatulence for eight years "not bad enough to worry about," and severe pain for four months, much worse one day. At operation an extensive

†In England and Wales in 1947, 7,851 male deaths and 6,243 female deaths were recorded as being due to carcinoma of the stomach.

area of induration 2½ in. (6.35 cm.) in diameter, and containing a large perforation ½ in. (1.27 cm.) in diameter was found in the pyloric antrum: the perforation was sutured. A test meal on May 20 revealed normal acidity, and gastroscopy on May 27 provided an excellent view of the antrum but no sign of an ulcer. It was, however, noted at the time that the pylorus was gaping slightly and that it might be a false pylorus due to spasm in the distal part of the antrum. Three weeks later, on discharge, the stools were still strongly positive for occult blood. He was readmitted on September 4, 1942, and died the same day. Post-mortem examination showed a huge ulcer crater on the lesser curve and anterior surface of the antrum, and direct infiltration of the liver. Microscopy showed carcinoma simplex.

Case 3.—A man aged 56 was admitted on September 22, 1942, with haematemesis and melaena. He had had epigastric pain two hours after meals for four weeks, and fifteen years previously had had a similar bout for four weeks. Both barium meal and gastroscopy indicated spasm in the pyloric antrum and it was noted gastroscopically that antral peristalsis was absent. A further barium meal on October 30 showed a fluid residue and a prepyloric deformity which "could be produced by a very large, shallow ulcer"; beyond this there was a duodenal ulcer. He was readmitted on November 6, when visible peristalsis was present. Perforation occurred on December 31, the day before a laparotomy had been arranged. At operation extensive thickening was found on the anterior surface of the antrum for 1½ in. (3.8 cm.) round a small perforation. Though there was some suspicion of a neoplasm at operation, the perforation was simply sutured and a gastroenterostomy performed. Gastroscopy on January 27, 1943, showed a medium-sized ulcer in the antrum that was thought to be benign. He was readmitted on March 15, when a mass was palpable in the right hypochondrium. He died on April 4, 1943. Post-mortem examination revealed an ulcerated carcinoma in the pyloric region of the stomach with small nodular deposits throughout the peritoneum. Microscopy showed a scirrhous carcinoma.

Case 4.—A man aged 49 was admitted on August 17, 1944, with a history of epigastric pain two hours after meals for eight years and sudden severe pain for one day. A duodenal ulcer had been found radiologically at another hospital two years previously. At operation a large ulcer was found on the lesser curve of the stomach 2 in. (5 cm.) above the pylorus, containing a small perforation; the perforation was sutured. A test meal on September 4 showed normal acidity, and at gastroscopy on the 6th there appeared to be an almost healed ulcer on the lesser curve of the stomach just above the angulus. He was readmitted on April 30, 1946, with a recurrence of pain for six months. A barium meal on March 28, 1946, had shown an ulcer on the lesser curve just in the pyloric antrum; this was confirmed gastroscopically. A further gastroscopy on May 21 showed scarring of the lesser curve of the antrum, but the ulcer appeared to be healed. He was readmitted on August 12 complaining of continual pain since discharge. At operation a large ulcer 2½ in. (6.35 cm.) in diameter was found near the lesser curve and adherent to the pancreas; there was also evidence of a healed duodenal ulcer. A partial gastrectomy was performed and microscopy revealed the presence of an adenocarcinoma. He died on February 17, 1947. Permission for a post-mortem examination was not obtained.

Case 5.—A man aged 34 was admitted on February 21, 1946, with epigastric pain after meals for eight months and severe pain for one day. At operation a large indurated ulcer was found high on the anterior wall, adherent to the under surface of the liver and containing a perforation ⅛ in. (0.3 cm.) in diameter. The perforation was sutured. A test meal on March 7 showed hyperchlorhydria, and at gastroscopy a week later no ulcer could be seen. He attended the follow-up department for three months, during which time he remained symptom-free, but when seen again on October 8, 1947, he complained of recurrence of pain for eight months. A barium meal at this time showed no abnormality. A further barium meal on July 31, 1948, revealed a large ulcer high on the lesser curve with distortion of the neighbouring mucosa suggestive of neoplasm, and he was advised admission. He failed to come into hospital until May 20, 1949, when a laparotomy was performed and a growth found just below the cardiac orifice infiltrating the left lobe of the liver. The stomach and part of the liver were resected and histological examination showed a scirrhous carcinoma.

Case 6.—A man aged 73 was admitted on December 13, 1946, with a history of epigastric pain two to three hours after meals for six months and sudden severe pain for six hours. At operation a perforation was found high on the anterior surface of the stomach near the lesser curve; the perforation was sutured. A test meal on January 4, 1947, showed achlorhydria. He was discharged on February 5 and was seen again in the out-patient department on September 6, 1948, when a mass was palpable in the epigastrium. A barium meal on October 1 revealed an extensive neoplasm of the fundus and body of the stomach with involvement of the lower oesophagus. He died on December 24, 1948, and post-mortem examination revealed a leather-bottle stomach, the whole stomach and lower 2–3 cm. of the oesophagus being involved.

Case 7.—A man aged 49 was admitted on August 14, 1947, with epigastric pain worse four hours after meals for six months, and severe pain of sudden onset for one day. At operation a large saddle-shaped ulcer was found on the middle of the lesser curve penetrating the pancreas posteriorly and with an anterior perforation ¼ in. (0.6 cm.) in diameter; the perforation was sutured. A barium meal as an out-patient on October 13 revealed a large ulcer on the middle of the lesser curve, above which there was an hour-glass constriction. He was readmitted on October 31, after one month's vomiting. At gastroscopy one week later there was seen to be an unusual mid-gastric constriction with a heaping up of the mucosa suggesting carcinoma. At operation on November 12 a gastric mass was felt, suggestive of carcinoma, but the patient's poor general condition prevented resection. He died on January 16, 1948, and at necropsy a scirrhous carcinoma of the pylorus was found, invading the pancreas and extending up to the middle of the body of the stomach, producing an hour-glass constriction at the upper end and pyloric stenosis at the lower.

Case 8.—A man aged 64 was first admitted on April 1, 1948, with four weeks' history of epigastric pain after meals and a palpable mass in the right hypochondrium. He refused investigation and was discharged with a clinical diagnosis of carcinoma of the stomach. He was readmitted on April 20 with severe pain of one day's duration. At operation a large perforated ulcer was found at the pylorus, which was considered to be benign and was therefore sutured. At gastroscopy on May 6, 1949, a large carcinomatous ulcer was seen on the lesser curve of the antrum. He at first refused operation, but eventually agreed, and a laparotomy was performed on August 3, when an inoperable carcinoma was found in the pyloric region of the stomach adherent to the liver and the pancreas.

Discussion

It is difficult to compare the results in this series with others, as most published series of perforated ulcers specifically exclude carcinomas. However, Judin (1937) recognized 3 carcinomas in 272 perforations. Raw (1944) 3 in 315, and Lenormant (1942) 10 in 185. A follow-up is not always reported in published series, and it is possible that the incidence of misdiagnosis has been, if not as high as the present one, at least appreciable. For example, isolated instances have been reported by Smets and Henrotin (1947) and by Williams (1944).

That misdiagnosis is easy is stressed in all the reports in the literature. Bisgard and Overmiller (1944) reviewed 217 perforated gastric carcinomas and found that the diagnosis had been made preoperatively in only seven instances. They commented that: "More astonishing was the failure, in the majority of instances, to recognize at operation that perforation had occurred in a carcinomatous crater instead of a benign peptic ulcer. . . . The failure to recognize the

presence of the carcinoma suggests that the majority of carcinomas which perforate are small and relatively confined lesions, presumably suitable for resection." Black and Blackford (1945) considered that it was often impossible to distinguish the two conditions macroscopically. It is therefore reasonable to believe that the present experience is not exceptional.

On the other hand, it may be said that these cases merely illustrate the difficulty that always exists in differentiating benign and malignant ulcers of the stomach—a difficulty much stressed in America. However, in our experience, patients who have presented with haematemesis or pain and in whom a confident diagnosis of simple gastric ulcer has been made have not returned with carcinoma as often as in the present series; it was because of the striking difference of the experience with perforated ulcers that the series has been collected.

Reviewing the cases individually, it seems that an error of judgment was made in two (Cases 2 and 3) and that two others were inadequately followed up (Cases 6 and 7). The remaining three, however, were watched until what appeared to be satisfactory healing was observed by gastroscopy, so that close follow-up is not in itself an adequate precaution.

Analysis by age and sex shows that the observed misdiagnoses were confined to men over 30. The literature does not generally record in detail the cases which were misdiagnosed at operation, most of the individually reported cases being those which the authors recognized as carcinomatous. Detailed records have been found in only four instances (Chapuy and Jeune, 1936; McKechnie and Priestley, 1937; Dickinson, 1939; Ives, 1949). These were all in men aged 40–60.

Carcinomatous perforations certainly occur in women—a quarter of Aird's collected series were female—but the type which is apt to be mistaken for a simple gastric ulcer has so far been reported only in men. A possible explanation of this sex difference may lie in the fact that simple ulcers are relatively more likely to perforate in men than in women; for example, the sex ratio for perforated ulcers shown in Table II is 12 : 1, whereas the sex ratio for all ulcers at the same hospital is 5 : 1 (Avery Jones and Pollak, 1945). It is possible that the early carcinoma creates an area of decreased resistance to peptic digestion and permits the development of a secondary simple ulcer in which perforation may be expected to occur on occasion as well as in the carcinoma itself. If this is so, the ease of misdiagnosis can be explained as well as the peculiar sex ratio.

Analysis by site is not helpful except in showing that the risk of carcinoma is present in all parts of the stomach, and that perforations near the greater curve should always be treated as malignant. In the four cases in the literature, mentioned above, the perforations were described as being at or near the pylorus; but it would be unwise to lay stress on this site to the exclusion of the rest of the stomach.

It can be concluded that, if errors are to be avoided, special attention must be paid to the whole group of perforated gastric ulcers in men. Increased awareness of the possibility of carcinoma may result in the recognition of some cases that would otherwise be missed, but if the hypothesis is true that early carcinoma may give rise to superimposed simple ulcers some errors will continue to be made. Even routine biopsy at the time of operation cannot be relied on, as carcinoma might not be present in all parts of the periphery of the perforation. Such an event has, indeed, been reported by Williams (1944).

There remains the possibility of treating the perforation by immediate gastrectomy. It is not desired to enter into a full discussion of the merits and demerits of this procedure, but it must be remembered that the stomach is more mobile and easier to resect in perforated ulcers, which are mostly anterior and in the distal half of the stomach. than it is in the average ulcer which comes to operation for intractable pain. Many large series of perforations treated by gastrectomy have been published. DeBakey (1940) collected 2,392 cases with a case mortality of 13.4%. Undoubtedly the patients subjected to gastrectomy were selected for their good initial condition, and it is not fair to compare these results with the average case mortality of 25.9% found by DeBakey for cases treated by simple closure. However, Judin (1937) was able to report a case mortality of 12.6% for a total of 418 perforations coming to operation, of which 75% were treated by immediate gastrectomy.

Since then, advances in surgery and anaesthesia have greatly reduced the mortality of perforations, but this is not an argument against the major procedure, the danger from which has been similarly reduced. When it is remembered that the case mortality of perforated gastric ulcers is greater than that for duodenal ulcers, that 50% have severe relapses and 20% further major complications within five years (Illingworth, Scott, and Jamieson, 1946), an appreciable added risk of carcinoma must make immediate resection worthy of serious consideration in the limited group of perforated gastric ulcers in men over 30.

Summary

Seventeen cases of perforated carcinoma of the stomach are reported. Eleven occurred among 452 persons operated upon for perforation of the stomach or duodenum; eight were initially considered to be benign.

Of 86 perforations in men, diagnosed as being simple gastric ulcers at operation, seven (8.1%) proved to be malignant within three years.

Post-operative investigation is not enough to ensure that malignant cases are recognized before discharge from hospital. and it is suggested that the risk of carcinoma is an important reason for considering partial gastrectomy as the treatment for perforated gastric ulcers in men over 30.

I am grateful to Dr. F. Avery Jones and my surgical colleagues for permission to publish these cases, and to Dr. F Avery Jones, Mr. J. D. Fergusson, Mr. T. G. I. James, and Dr. D. D Reid for advice in the preparation of the paper. I am also grateful to Miss B. White for her great help in the collection of the material

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PSORIASIS*

BY

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It is not possible here to offer an adequate survey of the problems—clinical, aetiological, and therapeutic—that psoriasis presents for our consideration. I propose, therefore, to discuss only my own viewpoint upon certain aspects of the disease.

The primary problem of psoriasis is to my mind identical with that of rheumatoid arthritis. Are these two conditions, which together may form the syndrome psoriasis arthropathica, due to specific infective organisms, no matter what other provocative factors may obtain, or are they non-specific reactions of the skin and of joint-structures, respectively, which may be elicited by a variety of agents in certain persons who may have an inborn or inherited tendency to react in this way?

I think one may with certainty exclude the possibility of psoriasis being due to a bacterium or fungus growing locally in the skin, and those who adduce the infective theory for the most part fall back on the filterable virus, as some have done in acute rheumatism and rheumatoid arthritis. Desaux (1948), who with others holds this view, has summarized the evidence in favour of it, but he also fully recognizes a number and a variety of adjuvant factors. It is tempting to argue that, since such factors may be entirely different in different cases, as they are in admittedly non-specific eruptions like eczema and urticaria, therefore psoriasis must be of non-specific causation. As I have previously pointed out (Barber, 1936, 1938), and as emphasized by Desaux, herpes simplex exposes the fallacy of this argument, since, although it is always directly caused by a virus, this may be activated by such diverse agents as other infections, drugs, foods, foci of reflex nerve-irritation, and the premenstrual and menopausal states. Moreover, as in psoriasis, correction of one or other of these provoking causes may prevent further attacks.

Up to the present time, however, in psoriasis the virus theory has not been established, and the arguments that plead in favour of the eruption being an inborn and often inherited mode of reaction of the skin to trauma and stress, using such words in their widest sense, are very strong.

To my mind, in fact, psoriasis has the hallmarks of a non-specific disease, whereas, by way of contrast, lichen planus has those of one due to a specific infective organism. It is significant that there is no specific treatment for psoriasis, whereas one cannot doubt the specific action of mercury and arsenic in lichen planus, although a few cases may prove resistant.

Psoriasis might well be classed with gout, rheumatoid arthritis, and rheumatic fever among the "allergic" group of diseases, but, since the word allergic has lost much of its original meaning, I prefer Hans Selye's term, "diseases of adaptation"—i.e., morbid reactions that result from the exposure of an organism to stress. By stress I imply such varied agencies as trauma, heat, cold, light, acute and chronic infections, drugs, physical and mental fatigue, and emotional disturbances.

I regard the patient work of Selye (1946) and his collaborators as an outstanding contribution to the elucidation of the non-specific diseases. It is, however, merely a sequel to that of earlier workers, which is often forgotten. In 1920, for example, Danysz described the following experiment:

"If, say, a dozen rabbits are injected daily or oftener with small doses of horse serum (0.01–0.1 ml.) for a period of some weeks, there will be no anaphylactic shock owing to the short intervals between the injections, and at the end of the course the rabbits will appear little or none the worse. If, however, they are kept under observation for the next few months they will gradually develop manifestations of chronic diseases, but whereas some present nervous symptoms, such as paralysis, in others skin eruptions with alopecia appear, and in others arthritis, and so on. At the end of a year the majority will have died in cachexia."

Now, to my mind, this experiment illustrates a fundamental attribute of chronic non-specific disease—namely, that, although the species of animal and the stress be exactly the same (in this instance respectively the rabbit and injections of an antigen, horse serum)—the tissue or structure that reacts to the stress may be entirely different in different individuals. This accords with our clinical experience of human beings. We may term the reacting tissue or structure the target-organ, which in one person may be the skin, in another the joint structures, in another the cardiovascular system, in another the gastro-intestinal tract, in another one or more endocrine glands, and in another the somatic or the autonomic nervous system. The stress may be the same, but its effects vary according to the reacting individual: one person, for example, developing arthritis, another arteriosclerosis or polyarteritis nodosa, another peptic ulcer, another alopecia areata, eczema, urticaria, or psoriasis, and another thyrotoxicosis. On the other hand, a person's target-organ may be affected by various stresses at different times, so that a given symptom may be evoked on one occasion by an acute infection and on another by an emotional upset or physical exhaustion.

We thus see that in the non-specific diseases the target-organ may be specific for the individual although the stresses that act upon it may vary at different times. We do not yet clearly understand what determines the vulnerability of a certain tissue in a given person. We speak of hypersensitiveness, and we know that this state may sometimes follow trauma of some kind, but much is obscure. There is, however, one factor that is obviously of immense importance—namely, heredity—and there may be a familial tendency to group reactions, as in the asthma–rhinorrhoea–eczema–prurigo–migraine syndrome, or to one reaction, as in cardiovascular disease, arthritic gout, and rheumatoid arthritis. A patient of mine with the severe generalized form of alopecia areata affords a remarkable example of the latter. In his case the alopecia followed a bombing incident. His mother developed it when he was nearly killed as a baby, her sister after the illness of her child, and her brother after an injury. In this instance, therefore, the same target-organ—viz., the hair papillae—reacted to emotional stress in four members of the same family.

I have no time even to summarize Selye's work and conclusions, but his pathological findings are similar to those described by Petit and Loiseau (1908) in horses immunized intensively for the production of antitoxic sera. Post mortem, these authors found, as Selye did long afterwards, profound changes in the lymphatic and reticulo-endothelial system, evidence of hypersecretion of the endocrine glands, and degenerative lesions in the liver and kidneys.

Selye's work is important because he has shown experimentally that, whereas some diseases are merely signs of

*Read in opening a discussion in the Section of Dermatology at the Annual Meeting of the British Medical Association, Harrogate, 1949.

damage due to lack of adaptation, others (e.g., hypertension, periarteritis nodosa, nephrosclerosis, and arthritis) may be the result of abnormal or excessive adaptive reactions to our environment. It is the pituitary–adrenal mechanism that is chiefly concerned in this over-adaptation, with the production of excess of salt-active corticoids by which lesions identical with those of periarteritis nodosa, nephrosclerosis, and acute rheumatic fever can be produced experimentally.

Since my paper was written the practical value of Selye's work has been suggested by the preparation by Kendall of 17-hydroxy-11-dehydrocorticosterone ("compound E"; cortisone) for the treatment of rheumatoid arthritis. Assessment of its permanent value is at present impossible, but it will be interesting to see whether it influences the psoriasis as well as the arthritis in cases of psoriasis arthropathica.*

It may be relevant to Selye's work that the relationship between psoriasis and adrenocortical hypofunction has been claimed by several observers, notably Grüneberg (1937), Kissmeyer, Chrom, and Jacobson (1935), and Incedayi and Ottenstein (1941). Reiss (1949) has recently reviewed this question and reported the results of laboratory investigations into evidence of disturbance of adrenal function in 25 cases.

Grüneberg had good results from injections of pituitary corticotropic hormone and cortin, particularly in arthropathic psoriasis, but Wise and Sulzberger were not successful with cortin alone.

Aetiological Factors in Psoriasis

I have said that in the present state of knowledge there is no specific treatment of psoriasis *per se*. As with all non-specific diseases, every patient presents a separate problem and his rational treatment will depend, after full investigation, upon consideration of the most likely provocative factors in his particular case. I deplore the habit among some doctors of informing their patients that psoriasis is incurable. Even if it were universally true it would be a cruelly unnecessary statement, and one might with equal justification say that asthma and peptic ulcer are incurable.

Heredity.—Widely different figures have been given regarding the frequency of a familial incidence in psoriasis. They vary from 15% to 63%, and we may take 30% as a conservative estimate.

Hereditary Associations.—There is apparently a familial association both with acute rheumatism and with rheumatoid arthritis. Dr. Elizabeth Hunt (1938) in a series of 75 cases of psoriasis found that 70% gave a family history of rheumatic manifestations and 30% of psoriasis. There is also a group of cases in which psoriasis appears to be a familial alternative to the allergic group of symptoms—asthma–eczema–hay-fever–migraine—as in the pedigrees recorded by Paterson and by Bettman, and quoted by Cockayne (1933).

Psoriasis in Relation to Age of Onset.—Broadly speaking, it may be said that psoriasis beginning in childhood usually presents the same aetiological problem as that of rheumatic fever. When it appears for the first time in adult life it may have to be considered in connexion with rheumatoid arthritis (psoriasis arthropathica); with focal infection (sometimes being associated with infective fibrositis or arthritis); with metabolic disturbances, particularly gout; with intestinal toxaemia and hepatic insufficiency; and with the menopause.

In sum, clinical experience and therapeutic results suggest that the problem of the provoking causes and of the rational treatment of psoriasis is in many cases the same as that of the heterogeneous group of so-called rheumatic diseases—in childhood rheumatic fever, in adults rheumatoid and infective arthritis, fibrositis, gout, and menopausal arthritis.

Sex Incidence.—On the whole males predominate in the ratio of about three to two, but Japanese figures give the ratio of seven to three. In pedigrees of families with no conductors the sex incidence is about equal, but in those with conductors males predominate strikingly (Cockayne) In one pedigree recorded by MacLeod (1920), however, nine members were affected out of 14 in four generations. the ratio of males to females being five to four.

Race Incidence.—Psoriasis is common in all European races and in Jews, less frequent among Asiatics, and very rare in pure negroes and even mulattos.

Climate and Season.—It is more frequent in cold and temperate climates than in warm countries, and rare in the Tropics. Like rheumatic fever, it is apt to begin or relapse in late winter and early spring, and to clear by late summer When associated with hay-fever it is usually at its worst in the pollen season.

There is one very significant fact brought out by Selye's experiments on the hormonal production of arthritis which may explain the influence of climate and temperature upon both rheumatism and psoriasis. He showed that, although it was easy to produce nephrosclerosis, hypertension, and periarteritis nodosa by injections of desoxycorticosterone acetate in animals placed on a high salt intake, arthritis very seldom developed. If, however, their heat-regulating mechanism were disturbed by thyroidectomy or adrenalectomy, arthritis occurred with great frequency, particularly if they were exposed to cold.

Psoriasis in Childhood

I am in agreement with Dr. Hunt (1933, 1938) and others that when psoriasis appears first in childhood there is usually an evident association with streptococcal infection of the throat. It often appears suddenly like an acute exanthem after tonsillitis or scarlet fever, and widespread exacerbations occur with subsequent attacks of tonsillitis. There is a latent period, usually of from 10 to 21 days, between the onset of the throat infection and the outbreak of acute guttate psoriasis, just as there may be in rheumatic fever between the sore throat and the development of arthritis and pericarditis or endocarditis. Dr. Hunt has emphasized the rarity of rheumatic complications, such as carditis and chorea, in those children who develop psoriasis—another example of the long-recognized protective function of the skin that I have discussed in connexion with the erythema group of eruptions (Barber, 1929).

In these juvenile cases of psoriasis the disease often, of course, persists into adult life, and one then usually finds a chronic infection of the throat, effective treatment of which may prove curative of the psoriasis. There are, however, cases of psoriasis in childhood in which there is no accompanying throat infection, and in a number of these the eruption may occur with, or appear to be an alternative to, the eczema–prurigo–asthma–rhinorrhoea group of symptoms.

*Recently Hench and his colleagues have observed the good effect of cortisone and ACTH on the psoriasis in such cases, and Spies and Stone have published a case in which ACTH was given (*Lancet*, 1950, 1, 11).

Psoriasis in Adult Life

As I have said, when psoriasis occurs for the first time in adult life there seems to be the same multiplicity of provoking factors that obtains in a medley of so-called rheumatic disease in adults. I do not wish to stress the association unduly, but one must admit it, I think, in psoriasis arthropathica and in gout with secondary osteoarthritis. I will first discuss the influence of infections upon psoriasis. Some acute infections, such as typhoid, lobar pneumonia, and measles, usually cause an existing psoriasis to disappear temporarily. Streptococcal infections, however, as a rule have the opposite effect, provoking as they do acute exacerbations, sometimes resulting in generalized exfoliative dermatitis. I have several times seen this occur in adults after tonsillitis, and twice after erysipelas.

I well remember the remarkable case of an alcoholic lady who had suffered from psoriasis and gout for many years. One evening she had a rigor and became acutely ill. It was soon clear that she had streptococcal septicaemia, and several positive blood cultures were obtained. Her psoriasis rapidly spread, and developed into a pustular and oozing exfoliative dermatitis. A fatal issue was expected, but she was treated by minute doses of an autogenous streptococcal vaccine, and eventually an enormous abscess developed in one thigh, the same strain of streptococcus being obtained from the pus. When this was evacuated she made a rapid recovery and remained free from psoriasis for some months, but it eventually relapsed in its usual form.

Another well-established example of the influence of streptococcal infection upon psoriasis is afforded by pustular psoriasis of the extremities. On this subject Clinton Andrews (1935), Ingram (1938), and myself (Barber, 1930, 1935) engaged in friendly backchat for some time, but it is now clear that the essential condition is a pustular or vesiculo-pustular "ide" eruption, occurring chiefly but not exclusively on the hands and feet, circulatory stasis being, as in papulo-necrotic tuberculides, a localizing factor. This was illustrated by a recent case in which the eruption was confined to the blue foot of a leg severely affected by previous infantile paralysis.

If the patient is an actual or a potential psoriatic the pustules arise in patches that, clinically and histologically, are psoriasis. In non-psoriatics the condition is a vesiculo-pustular eczematide, for which Clinton Andrews's term "pustular bacteride" is very apt. Both types of eruption usually arise insidiously, and are a sure indication of a chronic focus of infection somewhere; but occasionally the outbreak is acute, following as a rule a streptococcal infection of the throat. It is my experience that the principal though not necessarily the only source of infection is commonly the tonsils; and here I would stress that in several cases abscesses have been found in excised tonsils that clinically were not certainly infected.

Apart from this pustular form, there is a group of cases of non-pustular psoriasis appearing first in adult life in which focal infection in the teeth, nasal sinuses, or elsewhere seems to be the provoking cause.

Apropos of this relationship between streptococcal infection and psoriasis in some cases, the observations of Norrlind (1947) are of interest. It has been shown by Cecil, Nicholls, and Stainsby (1931), and confirmed by many others, that the serum from patients with rheumatoid arthritis agglutinates the attenuated strains of haemolytic streptococci isolated in this disease in very high dilution (95% of cases), whereas this was not so in 50 normal controls. Haemolytic streptococci from scarlet fever and erysipelas were also often agglutinable.

Norrlind examined the serum of 66 cases of psoriasis for such agglutinins, and obtained over 50% positive results, the highest agglutinin titres being found, as might be expected, in psoriasis guttata. Six of the positive cases had psoriasis arthropathica. Controls with patients having other diseases showed a much lower percentage of positive results.

Psoriasis Arthropathica

Since Bourdillon published his classical thesis in 1888 on psoriasis and arthropathies, both physicians and dermatologists have studied this syndrome. In the majority of cases the arthritis is of the rheumatoid or atrophic type, but in psoriasis arthropathica Garrod and Evans (1924) emphasized the frequent occurrence of attacks of intermittent hydrarthrosis, and there is another characteristic feature—namely, the early involvement of the terminal interphalangeal joints with severe psoriasis of the corresponding nails.

A most remarkable and extremely rare variety is that described by Bauer and Vogl (1931) and by Shlionsky and Blake (1936) in which very severe deformities of the extremities occur owing to osteoporosis. Phalanges may be totally destroyed and the hands shrunken to half their size. Dr. Forman kindly showed me a case of this kind recently.

The most striking laboratory finding in Shlionsky and Blake's case was the low serum calcium (8.74%), but the serum phosphorus was rather higher than normal. All the patient's teeth had fallen out early in her disease.

In psoriasis arthropathica of the usual type streptococcal focal infection is certainly the primary cause of both the arthritis and the psoriasis in some cases, but I regard it as only one of the possible stresses that may be responsible.

A lady who remained under observation many years developed acute multiple arthritis of the rheumatoid type almost simultaneously with extensive psoriasis. Dr. Douthwaite, who is no adherent of the doctrine of focal infection, saw her with me and agreed that a large number of infected dead teeth were probably responsible. These were removed one by one, each extraction causing acute exacerbations of both the arthritis and the psoriasis, with pyrexia, and eventually she made a complete recovery except for some deformity of a few terminal interphalangeal joints, with psoriasis of the corresponding nails.

I would again draw attention to a group of cases that may be legitimately labelled psoriasis arthropathica, the syndrome being psoriasis, gout, and osteoarthritic changes in the joints of the hands and feet secondary to gout. In two characteristic cases there was the same involvement of the terminal interphalangeal joints with severe psoriasis of the nails that is seen in the rheumatoid type of psoriasis arthropathica. Both patients were chronic alcoholics, and the blood uric acid was very high.

Another link perhaps between psoriasis and rheumatoid arthritis is afforded by the influence of pregnancy and of certain types of jaundice upon both diseases. It is well known that rheumatoid arthritis may improve dramatically and that psoriasis usually disappears during the course of pregnancy, but that both relapse after parturition. The same is true to a less extent during an attack of jaundice. No doubt these facts will eventually be explained by biochemists and throw light on the pathogenesis of the two conditions.

Psoriasis and Metabolic Errors

I shall not attempt even to summarize the volume of literature on this subject. I am satisfied, however, that the association of psoriasis and gout is as well established an entity as psoriasis and atrophic arthritis. This is an

important practical point, since when the syndrome exists the eruption responds to rational treatment. Arthritic gout and tophi are not necessarily present in such cases, but a history of attacks of podagra in the past may be obtained, and, as Hench says of undoubted gout, hyperuricaemia is usually but not necessarily present. I have already referred to the gouty type of psoriasis arthropathica. One of my best examples was the son of a father crippled with long-standing gout and a psoriatic mother. His only sister had psoriasis, but not gout.

Just as psoriasis may replace keratoderma climactericum, so hyperkeratotic psoriasis may be substituted for the gouty form of palmar and plantar keratoderma.

The theory that psoriasis is due to an error of fat metabolism—in fact, a lipoidosis comparable to xanthomatosis—as suggested by Grütz and Burger (1934), and that there is an increase of lipoids in the skin, is unacceptable. I can personally confirm the findings of Dodds, MacCormac, and Robertson (1942) that the serum cholesterol and the response to ingestion of cholesterol may be normal. With regard to carbohydrate metabolism, certain cases of congested irritable psoriasis are found to have hyperglycaemia and they improve on a low carbohydrate diet, but, as with other metabolic disturbances, the findings of glucose-tolerance tests are inconstant.

Dr. Whitfield has stated that in psoriatics in whom intense indicanuria was found the eruption often responded dramatically to intestinal antiseptics—creosote, dimol, or cyllin. I can confirm this observation in some degree, and in several cases have found a high proportion of non-lactose-fermenting coliforms in the stools, with evidence of hepatic insufficiency.

In this connexion the impossibility of relieving psoriasis in alcoholics with liver damage unless they abstain from alcohol may be mentioned.

Psoriasis and the Menopause

So far as we know no constant metabolic errors are found in psoriasis, and in most cases there is little or no clinical evidence of any endocrine abnormality. Nevertheless the climacteric, like pregnancy, has an undoubted though unexplained influence upon it. Here it must be emphasized that the climacteric is not a transient phase of short duration, since the hyperactivity of the anterior pituitary that results from the release of the ovarian brake may continue for many years. Psoriasis may appear for the first time at the menopause, or a long-standing psoriasis may be profoundly modified by it, chiefly in respect of its distribution.

As I have stated elsewhere (Barber, 1946), at and after the menopause psoriasis tends to desert the more usual sites on the extensor surfaces of the limbs and seek what I have termed the menopausal areas—namely, the groins, pubic region, vulva and internatal cleft, the umbilicus, the submammary folds, the axillae, the rosaceous area of the face, the sides and nape of the neck, and the palms and soles. This distribution in part is also adopted by eczema, neurodermatitis, and lichen planus in the menopausal and post-menopausal states.

There is another observation which illustrates again that psoriasis is a mode of reaction of the skin of certain persons under the influence of various determinants: the eruption may replace the simple hyperkeratosis of keratoderma climactericum, the common neurodermatitis of the nape of the neck, and the more usual secondary papulo-pustular eruption in rosacea.

Psoriasis and Psychological Disturbances

It is very difficult to appraise the influence of emotional disturbances in psoriasis. As with other chronic diseases, it is a question of the cart and the horse—that is to say, one has to determine whether the eruption was primarily evoked by psychological stress or whether the fact that the patient is a psoriatic is responsible for his mental depression. As Wittkower (1948) rightly says, "psoriasis is not bound to any one personality type, either physically or mentally." This is in striking contrast to the asthma-eczema–prurigo–rhinorrhoea syndrome, sufferers from which usually have a distinctive physical and psychical constitution.

That in a psoriatic a sudden shock may precipitate an acute exacerbation with a resulting generalized exfoliative dermatitis is certain, and I have seen it happen more than once; and all of us have observed the baneful influence of anxiety upon the disease.

Psoriasis and Food Allergy

What might prove a fruitful field of research is the question whether psoriasis is sometimes a cutaneous reaction to food allergy, and it is surprising that it has been neglected.

I have met with two cases in which cow's milk undoubtedly appeared to be the provoking cause. The first was that of a lady whom I had treated without much success for psoriasis and who years later returned to consult me for another reason. On inquiry she said she had discovered the cause of her psoriasis—namely, milk. She had had skin tests performed by the late Dr. Bray for migraine, and on his advice she omitted milk entirely from her diet. To her surprise the psoriasis disappeared, only to return when she took milk again. She had repeated the experiment more than once, and did so again at my request.

The second case was that of an infant seen with Dr. Tillmann. It had widespread and quite characteristic psoriasis—the youngest case I have seen. The eruption had appeared after the child was weaned on to cow's milk. On my advice "almata" made without milk was substituted; the psoriasis promptly cleared, but it returned when cow's milk was resumed. Unfortunately owing to the war we lost touch with the case.

Conclusion

To sum up, I have approached the problem of psoriasis purely from the clinical standpoint, although I have referred to findings of laboratory workers that seem to me relevant to its ultimate solution. I may be wrong in regarding psoriasis as a non-specific cutaneous reaction, but, whether it is or not, it certainly behaves like one. The sum total of clinical knowledge of non-specific diseases, collected and recorded by succeeding generations of physicians, is enormous, and during recent years, thanks to laboratory workers, much that was not understood has been explained. Nevertheless there are wide gaps in our knowledge.

If I have stressed my appreciation of the work of Hans Selye and his collaborators it is because it seemed to me that he began at the beginning and patiently studied the systemic effects of different kinds of injury on the living organism, as his master, W. B. Cannon, did before him. I believe that Selye's "alarm reaction" and "adaptation syndrome" afford the basis upon which the eventual understanding of these diseases and their treatment will be founded.

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SCIATIC PARALYSIS IN NEWBORN INFANTS*

BY

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Twenty cases of unilateral sciatic paralysis, sometimes accompanied by cutaneous gangrene of the ipsilateral buttock, have been seen in newborn infants in the maternity departments of two hospitals in Liverpool. In Hospital I, the maternity department of which has about 700 deliveries each year, three cases of sciatic paralysis occurred during 1945. In Hospital II, with an average of 3,000 deliveries annually, 17 cases of sciatic paralysis were recorded during the period from April, 1945, to June, 1948. Eleven of these cases have been studied by Fahrni (1950). The purpose of this paper is to record the development of further cases and to suggest a probable theory of causation.

Clinical Picture

Two cases are here described in detail, and the salient features of all the cases are summarized.

Case 1.—A male infant weighing 8 lb. 1 oz. (3.7 kg.) was the first child of a healthy mother aged 28. Labour took place at term and lasted 32 hours. The head presented in the left occipito-anterior position and the infant was born with the cord tightly around the neck and in a state of asphyxia pallida. Routine measures of resuscitation were employed and recovery was prompt. Before the infant left the labour ward the right leg was noticed to be white and the right buttock of a bluish colour. On the following day the right leg was still pale and there was complete foot-drop.

Case 2.—A male infant weighing 5 lb. 3 oz. (2.4 kg.) was the first child of a healthy mother aged 22. Labour lasted 22 hours and the head was delivered in the left occipito-anterior position after an episiotomy. The infant was in a state of asphyxia pallida, but responded well to routine measures of resuscitation. "Bruising" of the left buttock was noticed on the day of birth. Next day the discoloration extended from the iliac crest to the inferior gluteal fold, crossing the midline slightly in the perineum only. There was a flaccid paralysis of the calf muscles and peronei, but the quadriceps and hamstrings seemed normal. The discoloration changed to a hard black necrotic area, less extensive than the original bruising and having a clearly marked hyperaemic margin (see photograph). A central slough gradually peeled away, leaving a clean granulating ulcer. After six and a half weeks a healed scar remained, and there was also complete foot-drop on the same side. At the age of 6 months movement of the toes and ankle was fairly good, but the left foot was colder and ½ in. (1.25 cm.) shorter than the right foot.

Case 2. The hard black necrotic area eight days after birth.

In the 20 cases observed the mothers of the affected infants were of various ages and parity. All had normal pelves and were healthy during pregnancy. Delivery was by vertex presentation in all but three cases, one infant being delivered by lower-segment caesarean section and two by breech extraction. In every case but one asphyxia at birth was recorded.

The left leg was affected in 14 cases and the right in six. Paralysis was usually noticed during the first 24 hours, but in some cases it was not recorded until the second day. The most obvious and persistent feature in all the affected babies was foot-drop. Movement has improved gradually during the first six or nine months, and in a few instances recovery has been complete. In the majority of cases some degree of foot-drop has remained and growth of the foot has been retarded. The late appearance resembles that of poliomyelitis, and some of these infants will require operative orthopaedic treatment to correct shortening and equinovarus deformity. All have been kept under supervision and have received physiotherapy.

Gangrene developed in the buttock of the affected leg in six cases; its first indication was a bluish mottling of the skin, often noticed in the labour ward. In two or three days the discoloured area had a sharply defined serpiginous margin and the centre was bluish red, often with small white patches; at the periphery there was a narrow red band. The lesion was not raised, but on palpation felt hard. Gradually a black slough peeled away, leaving a deep ulcer and finally a permanent scar. In one other

*This article is based on a paper read by one of us (F. P. H.) before the Liverpool Paediatric Club on April 22, 1949.

case the initial discoloration appeared to be fading when the infant was taken home against advice on the tenth day.

Two infants had generalized muscular twitchings suggestive of cerebral asphyxia or trauma. The convulsions ceased in 48 hours and there was no evidence of cerebral damage after six or nine months.

Discussion

Paralysis of one or both legs in a newborn infant may follow a difficult breech delivery, due to stretching of the lumbosacral plexus or to damage to the spinal cord; but such injuries are rare. Morgan (1948) has described radial nerve paralysis in the newborn caused by the intrauterine pressure of a contraction ring. Gangrene of an upper left extremity in a newborn infant has been described by Steiner (1945). In this case gangrene began in the fingers and progressed to the forearm so that amputation was eventually required. Trauma during delivery was thought to be the cause, the arm having prolapsed and become compressed between the child's cranium and the mother's bony pelvis.

It is of interest to note that in 39 cases of gangrene affecting the extremities of newborn infants reviewed by Heller and Alvari (1941), labour was "difficult" in 11 cases, the cord encircled the neck in two instances, and asphyxia was present in eight cases. Paralysis of the affected limb preceded the onset of gangrene in the case described by Steiner and also in a case described by Heller and Alvari.

Various causes for the lesions we have described must now be considered.

1. The adoption of some unusual method of resuscitation by a particular midwife has been suggested, but can be ruled out by the frequent changes of staff in the labour wards.

2. No prominent ridge was found on the resuscitation table which might have damaged the delicate tissues of a newly born infant.

3. A misplaced injection of vitamin K which might conceivably damage the sciatic nerve and the skin of the buttock. When an oily preparation of the vitamin was used in Hospital II, an abscess sometimes occurred at the site of injection, but paralysis or cutaneous gangrene was never recorded. Since September, 1947, a watery preparation has been used exclusively, and it has not been known to cause any ill-effects. Cases of sciatic paralysis continued to occur after the use of vitamin K by injection had been entirely stopped.

4. One of us (A. G. O'M.) suggested that "cycliton," the analeptic in regular use in Hospital II, might have been injected into an umbilical artery in mistake for the vein. When we were investigating this possibility Mills (1948) reported somewhat similar cases which he attributed to the injection of nikethamide ("coramine") into an umbilical artery. He has since reported the series in detail (Mills, 1949), and we agree in general with his conclusions. Bates and Page (1949) have recorded one similar case in which nikethamide was used as an analeptic. In 19 of our 20 cases asphyxia at birth was recorded, and cycliton, 0.3 ml. to 1 ml. was injected into a cord vessel. In one case, however, there was no record of asphyxia being present or cord injection being given, and if our theory is correct it seems probable that a busy midwife had omitted to note the fact on the case sheet.

The effects of intra-arterial injections of potentially dangerous or irritative drugs have been carefully studied by Cohen (1948). He discusses 12 cases in which the accidental intra-arterial injection of thiopentone in the antecubital fossa had serious effects. The clinical results included pallor and cyanotic mottling of the skin distal to the site of injection, paralysis, and sensory changes in the forearm and hand, and often an extensive peripheral gangrene which necessitated amputation. Most striking of all, he describes in detail patches of cutaneous gangrene which closely resemble those which we have seen. In most of the cases described by Cohen, intra-arterial thrombosis was found when arteriectomy was performed (in one case as early as 50 minutes after the injection) or on dissection of an amputated limb.

Gammel (1927) reported necrotic lesions in the skin of the buttock after injections of bismuth and differing in character from the deep-seated abscess which may follow an intramuscular injection. In one of his cases there was also peroneal nerve paralysis. He was able to find about 30 reports of similar conditions following injection of mercury or bismuth preparations. One observer had made a biopsy of the skin lesion and had found that the cutaneous arterioles were blocked with crystals of bismuth salicylate. This important finding was confirmed by animal experiment. The inference is that the drug had been injected into a deep artery, possibly the inferior gluteal, and had caused local emboli.

Clinically the lesions we have described were comparable with others in which intra-arterial thrombosis has been demonstrated. This possibility must now be examined from the anatomical, physiological, and pharmacological aspects.

In the foetus the blood supply to the lower limb is carried by the sciatic artery, the main branch of the internal iliac artery, and the external iliac artery is a purely subsidiary blood supply. After birth this function is reversed: the main blood supply is gradually taken over by the external iliac artery, and the sciatic artery becomes quite a small vessel, functioning mainly as the nutrient artery of the sciatic nerve.

In asphyxia neonatorum of severe degree the umbilical vein, like other veins, will be collapsed. It is therefore conceivable that an injection into the cord may be given into one of the two umbilical arteries. This fluid will pass down to the hypogastric artery and so to the internal iliac artery and the sciatic artery. If such a fluid caused arterial spasm, followed by thrombosis, the blood supply to the sciatic nerve and to the buttock would be jeopardized.

Nerves have a regional and longitudinal blood supply. They receive twigs from any near-by artery, and those twigs divide in the substance of the nerve to form a longitudinal anastomosis. The latter is said to give nerves a relative independence from the regional supply. In the case of the sciatic nerve, however, Adams (1942), referring to work done on the blood supply of the nerve, says, "The results are convincingly in favour of the dominance in this nerve at least of the regional over the longitudinal." He also points out that degeneration of the sciatic nerve in a rabbit has been produced by ligation of the inferior gluteal artery. One infant died from enteritis, giving the opportunity of sectioning the sciatic nerve. At the level of the slough there were recent haemorrhages into the nerve fascicles, while distal to it the circumference of the fascicles was waxy, suggesting shrinkage. Wallerian degeneration was not seen, probably because an ischaemic nerve with complete anatomical continuity between cell body and axis cylinder still persists, Wallerian degeneration being due essentially to a structural interruption in the continuity of the axis cylinder.

Cohen suggested that the ill-effects of intra-arterial thiopentone might be due to its alkalinity. It has a *p*H of 10.4–10.6. Cycliton, in contrast, is acid (*p*H 4.92) and coramine also (*p*H 5.77). It is unlikely that the acidity plays a significant part in causing these lesions, as no ill-effects have followed the use of lobeline (*p*H 4.80) as an analeptic. Lobeline, however, is an alkaloid obtained from *Lobelia inflata*, while the other two drugs are

synthetic compounds of a similar structure. Nikethamide (coramine) = pyridine-β-carboxylic acid diethylamide. Cycliton = diethylamide of 3:5-dimethyliso-oxazol-4-carboxylic acid.

No information has been obtainable about the detailed pharmacological action of cycliton. Faust (1925) has shown that nikethamide causes vasoconstriction by local action on the vessels, a property not found when Curtis and Wright (1926) investigated lobeline. Possibly the vasoconstriction produced locally by cycliton, associated with the vasoconstriction and slowing in arterial blood flow that accompanies asphyxia, precipitates the development of thrombosis. Beyond this we can only say, as Cohen does of thiopentone, that the arterial intima appears to be particularly sensitive to cycliton.

An attempt to reconstitute the lesion in animals was made by Professor R. A. Gregory (Department of Physiology). One millilitre of cycliton was injected into the internal iliac arteries of six adult cats, under light ether anaesthesia at aseptic operation, with negative results. The experiments were then repeated, but before injecting the cycliton the animals were kept in a state of asphyxia. Again the results were negative. Finally, in order to make conditions as comparable as possible to those obtaining in the newborn infant, small amounts of cycliton (0.05–0.5 ml.) were injected into the umbilical arteries of four newborn kittens; none of these animals survived longer than 24 hours.

Summary

Twenty cases of unilateral sciatic paralysis in the newborn, sometimes accompanied by cutaneous gangrene, are described. Accidental injection of cycliton into an artery instead of the vein in the umbilical cord is suggested as the possible cause of the lesions.

Experimental proof is as yet lacking, but the evidence in favour of this theory is as follows:

1. The cases occurred only in the hospitals in the city of Liverpool in which cycliton was in use.

2. The only common factors were asphyxia at birth and injection of cycliton into a cord vessel.

3. The lesions are consistent with the results of ischaemia due to disturbance of blood flow in the internal iliac artery, and are comparable to the lesions produced by intra-arterial injection of thiopentone.

4. No further lesions have occurred since cycliton has ceased to be used. (Cycliton is not now sold in England, although it is used extensively on the Continent and in other parts of the world.)

We would like to thank Professor R. A. Gregory for the considerable amount of thought and time that he has given in an attempt to establish experimental evidence, and Professor N. B. Capon and Mr. Bryan McFarland for their interest and help in the preparation of this article. We also wish to thank Professor T. N. A. Jeffcoate for permission to publish three of the cases, and Dr. S. E. Keidan (paediatric registrar) for his interest in the problem and help in recording the clinical details of many of the cases.

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ANAPHYLACTOID PURPURA IN PULMONARY TUBERCULOSIS

BY

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The occurrence of purpura in association with pulmonary tuberculosis is generally considered to be a rarity. Instances of it in sanatoria reports are not common, and references to it in the literature do not seem to be numerous, most of them appearing in publications from other countries. In view of this we feel it justifiable to report five cases which all attended a general medical clinic within the space of twelve months.

The association of purpura with pulmonary tuberculosis was described as early as 1801 by Willan in his treatise on cutaneous disease. He had noted the occurrence of purple spots in the skin in the last stages of pulmonary consumption, and considered it to be a forerunner of death. In contradistinction to this, in 1890 Rendu described a purpuric eruption especially prone to occur on the dorsum of the hands and wrists, which he considered was a premonitory sign of tuberculosis. Sixteen years later Bensaude, Carnot, and Harvier reported a case of purpura as a pretuberculous manifestation. In that year also, Bensaude and Rivet (1906) produced their monograph on this subject. They have classified four main groups: (1) Purpura haemorrhagica occurring in the course of miliary tuberculosis—and this was more common if the miliary state was superimposed on chronic disease. (2) Purpura haemorrhagica occurring in the course of chronic pulmonary tuberculosis, usually in terminal and cachectic states. (3) Purpura haemorrhagica occurring in the course of latent tuberculosis. (4) Purpura haemorrhagica occurring in the course of extrapulmonary tuberculosis.

They also considered that purpura may occur as a pretuberculous manifestation, though they did not classify it as such, and they stress the importance of searching for a tuberculous focus in the presence of chronic or recurring purpuric eruptions. Single cases found in the literature—such as that of Gossner, who reported the occurrence of purpura in a man with a tuberculous testis, the eruption disappearing with the removal of the organ—can be fitted into the classification.

The gravity of purpura as a symptom in pulmonary tuberculosis was stressed by Cruice (1912), who considered that it marked either a terminal stage or an exacerbation from which the patient might die, or if recovery occurred the state of the lesion would be found to be more advanced.

The purpura may be due to a symptomatic thrombocytopenia, be a simple symptomatic purpura, or be of the Henoch–Schoenlein group. The last-mentioned form is suggested by Bauch (1916). Witts (1946) considers that in all cases the endothelial lining of the vessels is damaged, and states that the platelet count varies from case to case. Greengard (1931), in his review of two cases, also considered capillary damage to be the most important factor in its development.

Case 1

A man aged 44 was admitted to hospital from the out-patient department. He gave a history of heaviness in the abdomen associated with nausea and loss of appetite of nine days' duration. Two days before admission he had noticed a generalized

rash on his legs, and next day had had severe colicky abdominal pain, with the passage of black motions, and his urine had become dark. He gave a history of bronchitis followed by pleurisy in 1936, since when he had had a slight cough, particularly in winter-time. Three months before admission he had had a small haemoptysis, but as he had felt well he had taken no notice of it.

On examination he looked thin and unwell, his temperature was 100.6° F. (38.1° C.), pulse 92, and respirations 20. Extensive areas of purpura were present over both legs with small purpuric spots on the thighs and arms. Percussion and air entry were impaired, and rales were heard at the right apex. No other abnormalities were found. A blood count showed: haemoglobin, 95%; red cells, 4,800,000; white cells, 18,300 (polymorphs 79%, lymphocytes 19%, monocytes 2%). The bleeding-time was four and a half minutes, clotting-time nine minutes, and the platelets numbered 240,000. Hess's capillary fragility test was strongly positive. The urine contained albumin and red blood cells, and the stools altered blood. The bone marrow was completely normal and the Wassermann reaction was negative. A radiograph of the chest revealed tuberculous infiltration at the right apex and mid zone with possible cavitation. Two cavities were demonstrated by tomography. The sputum contained tubercle bacilli, and the erythrocyte sedimentation rate was 60 mm. in the first hour.

Progress.—The patient was given complete rest in bed, and in the course of the next 48 hours the melaena ceased, the purpura disappeared in five days, and the haematuria stopped in ten days. By the end of a fortnight the temperature had settled, the leucocyte count was normal, and the erythrocyte sedimentation rate had fallen to 40 mm. in the hour. He was then transferred to a sanatorium, where after six months he was discharged symptom-free and feeling well; he has since resumed work.

Case 2

A woman aged 31 was seen in the out-patient department complaining of recurrent areas of discoloration of the skin of the legs for the preceding six weeks. Associated with the eruptions was cramp-like pain in her calves. At the onset she had also had severe colicky abdominal pain and had vomited a small amount of blood on two occasions. This condition had improved spontaneously after one week. She gave a history of pulmonary tuberculosis for the preceding four years, and had been discharged from a sanatorium some fifteen months previously.

On examination extensive purpura involving both legs and thighs was seen. The chest showed signs of consolidation at the right apex. Other systems were normal. The blood count was: haemoglobin, 84%; red cells, 5,000,000; white cells, 9,800 (normal differentiation). The bleeding-time was four minutes, the clotting-time eight and a half minutes, and there were 270,000 platelets. Hess's capillary fragility test was strongly positive. The urine contained albumin and red blood cells. A radiograph of the chest revealed chronic tuberculous infiltration at the left apex and mid-zone and the right mid-zone, while the trachea was displaced to the right. The right apical zone was completely opaque, probably owing to tuberculous consolidation. The sputum contained a large number of tubercle bacilli. The patient's general condition rapidly deteriorated, and after a short time she left the district to be looked after by relatives.

Case 3

A man aged 47 complained of a rash on both his legs which had first developed seven weeks previously, and had varied in intensity from day to day. At the onset he had had severe pain and swelling of the right knee and then of the right ankle, which lasted for two weeks, and some three weeks later both wrists had been similarly affected. He gave a history of pneumonia in 1948, but nothing else was relevant.

On examination an extensive purpuric eruption was seen on the legs, thighs, upper arms, and the lower part of the trunk. Both wrists were swollen and had limited movement. General examination was negative. A blood count showed: haemoglobin, 87%; red cells, 4,200,000; white cells, 7,500 (normal differentiation). The bleeding-time was three minutes, the clotting-time eight minutes, and there were 190,000 platelets. Hess's capillary fragility test was negative. A radiograph of the chest revealed several calcified foci in the left lung, with calcification in the corresponding glands. A soft opacity was present at the left apex and was thought to represent active tuberculosis.

Progress.—The purpura disappeared in one month without specific therapy. At the end of two months his platelets had risen to 270,000 and the erythrocyte sedimentation rate was 3 mm. in the hour. A chest radiograph was unchanged. When seen at the end of a further six months he was feeling well, had not had any further purpura, and had gained 5 lb. (2.3 kg.) in weight. The chest radiograph showed calcification in the opacity at the left apex, and the blood count was normal.

Case 4

A man aged 53 was referred to the out-patient department following the sudden development 24 hours previously of extensive purpura involving his legs, arms, face, and mouth. He felt well in himself, but for many years had been subject to a cough with sputum, which had become rather worse in the past winter. On account of this cough an *x*-ray examination of his chest had been made by the tuberculosis authorities three years previously and had revealed a calcified focus which was said to be inactive.

On examination he looked ill and was very thin. There were large bullae containing blood on both lips, with smaller ones on the tongue and on the mucous membrane of the mouth. The face, arms, and legs showed a widespread fine purpuric eruption with several larger areas of bruising about the size of a shilling. General systems were normal. The blood count showed: haemoglobin, 92%; red cells, 4,600,000; white cells, 5,400 (normal differentiation). The bleeding-time was two minutes, the clotting-time four minutes, and the platelets numbered 150,000. Hess's capillary fragility test and the blood Wassermann reaction were negative. A radiograph of the chest revealed tuberculous infiltration of both apical zones, some showing calcification. The sputum contained tubercle bacilli. The erythrocyte sedimentation rate was 10 mm. in the hour.

Progress.—The purpura started to go at the end of one week and had disappeared in a further 14 days. His general condition remains unchanged.

Case 5

A man aged 67 was admitted as an emergency case. He gave a history of loss of weight and cough for three months. In the two days before admission he had lost his appetite, had felt very ill, and had at times been irrational.

On examination he was seen to be a thin, pale, cyanosed, dyspnoeic man who was apyrexial. The chest showed signs of cavitation at the right apex, with consolidation of the rest of the right lung. A purpuric eruption, consisting of large reddish-purple blotches, was present on the dorsum of the hands, wrists, and forearms. A radiograph of the chest revealed cavitation at the right upper zone and patchy bronchopneumonic changes throughout the right lung field and in the left upper zone. The sputum was positive for tubercle bacilli. The blood count showed: haemoglobin, 52%; white cells, 16,100 (87% polymorphs). The bleeding-time was one and a half minutes, the clotting-time four and a half minutes, and the platelets numbered 190,000. Hess's test was negative. There was no microscopical haematuria, and the blood urea was 42 mg. per 100 ml.

Progress.—The patient rapidly deteriorated, and died in 10 days. The necropsy confirmed the pulmonary finding. There was no evidence of endocarditis. The liver and spleen were normal. The left kidney contained several infarcts.

Immediately before the development of the purpura none of the cases had been receiving any medication.

Discussion

In all cases the diagnosis of pulmonary tuberculosis was made on the radiological findings and was confirmed by the presence of tubercle bacilli in the sputum of all except Case 3, in which no sputum was obtained. The first four cases presented as extensive purpuric eruptions requiring diagnosis. In Case 2 only was there a definite previous history of tuberculosis, although Case 1 had had a haemoptysis three months before and Case 4 had been investigated for tuberculosis three years previously and the lesions then found were thought to be healed. In Case 5 the presence of purpura in association with the clinical findings in the chest pointed to tuberculosis as the likely cause, and this was subsequently confirmed.

In the first three cases the platelet count was within normal limits, and in the last two it was only just below the lower limit of normal. Consequently, it does not seem likely that thrombocytopenia could have been responsible. The appearance of arthritis and the occurrence of haemorrhages from the bowel and haematuria in some cases led us to consider that this purpura was allergic in nature.

The importance of capillary damage as a mechanism was borne out by the strongly positive capillary fragility test in the two cases that had gastro-intestinal bleeding and haematuria. These cases would seem to belong to the type described by Henoch, while Case 3 belongs to the Schoenlein type. With the exception of Case 5 the general condition of the patients was good when they were first seen, and their blood counts were within normal limits; this strengthened our belief that it was a sensitivity manifestation rather than a toxic effect in the bone marrow.

The findings in this small series do not support the suggestion of Cruice that the development of purpura is either a terminal condition or one marking a serious exacerbation. Only two of the five cases described showed marked deterioration, although Case 1 seems to have had a temporary progression of his pulmonary lesion. The two remaining cases had few signs of activity, being afebrile, with normal erythrocyte sedimentation rates, and evidence of subsequent calcification ensued without treatment.

The continuance of their general well-being, with quiescence of the lesion in two cases and only very transient deterioration in a third, supported the suggestion that toxaemia was unlikely.

Summary

A brief review of the literature on the occurrence of purpura in pulmonary tuberculosis is given.

Five cases of purpura occurring in the course of pulmonary tuberculosis are described in which the bleeding involved not only the skin but also the gastro-intestinal tract and kidneys.

In two cases the appearance of the eruption does not seem to have been the grave omen that the literature would have us believe.

These cases stress the importance of searching for a tuberculous focus on the incidence of unexplained purpura, as originally suggested by Bensaude and Rivet in 1906.

We wish to thank Dr. D. H. G. MacQuaide for permission to report these cases and for helpful advice in the preparation of this paper.

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Medical Memoranda

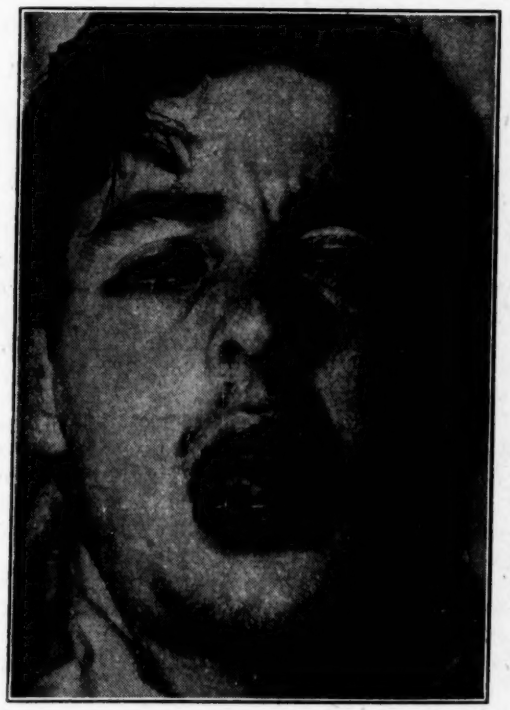
A Case of Stevens–Johnson Syndrome

This syndrome was first noted by Alibert and Bazin in 1822, and was described in 1922 by Stevens and Johnson, who recorded two cases. Few cases have been recorded in Britain; the majority have appeared in American and Canadian journals. Inquiry among colleagues, however, leads me to suppose that the condition is commoner than the number of recorded cases suggests.

Case Report

On September 17, 1948, a young man aged 20 was admitted with severe malaise, sore throat, cough, and haemoptysis. Twelve days previously he had contracted a cold, with sinusitis and a productive cough. Two days before admission he had a feeling of constriction in the chest and roughness in the mouth, and his face and eyes became swollen. The following day he had a rigor, and his symptoms became worse. On the day of admission he had itching of the legs, and his sputum became offensive and heavily blood-stained.

On examination he was seen to be extremely ill. His temperature was 102.6° F. (39.2° C.). The lips and buccal mucous membrane were excoriated and covered with white pseudo-membrane. The gums were ulcerated and bleeding (see Figure). There was bilateral conjunctivitis, with a film of



The patient on admission.

pus covering the right eye; the left pupil was smaller than the right. Both pupils reacted sluggishly to light and accommodation, and there was nystagmus to the right. A maculo-papular eruption was present on both lower limbs, the right forearm, and the left wrist. The papules varied in diameter from 0.25 to 1 cm., and were surrounded by a purplish-red areola. In both lungs there were signs of patches of consolidation. The liver and spleen were not enlarged. The knee-jerks, ankle-jerks, and abdominal reflexes were absent; all other reflexes were present and equal. Sensation was unimpaired. Swabs from the throat, gums, and conjunctiva yielded no growth on

culture. Smears from the gums showed fusiform organisms and *Treponema vincenti*. Sputum yielded a moderate growth of *Str. haemolyticus*. The w.b.c. numbered 14,000, of which 78% were polymorphs.

Treatment.—The patient received 100,000 units of penicillin intramuscularly four-hourly for 13 days. Tablets of sulphamezathine, 1 g. four-hourly, were also given for eight days. The eyes were cleaned with saline, and eye-drops of sulphacetamide sodium (10%) instilled hourly. Zinc and castor-oil cream were applied to the lids. Fifteen minutes before each meal the throat was sprayed with 1 in 3,000 "percaine" in glycerin. After the meal the tongue, palate, and throat were swabbed with 50% hydrogen peroxide and a dilute solution of citric acid. The lips were cleaned with an antiseptic and covered with boracic ointment. Four days after admission 0.1 g. of "anthisan" was given twice daily for five days.

Progress.—The temperature fell gradually to normal after 12 days. Conjunctivitis cleared a week after admission, by which time the reaction of the pupil to light and accommodation was normal. On September 18 a urethral discharge appeared, but ceased within 24 hours; it recurred on September 22, however, lasting eight days. On September 18 large vesicles, later becoming pustular, appeared on the glans penis. The rash spread on the original sites until September 24, but both the cutaneous and the oral lesions had practically disappeared by September 30. On September 26 the abdominal reflexes and ankle-jerks were normal, but the knee-jerks were weak. The cough, sputum, and haemoptysis persisted unchanged until September 24, after which there was improvement, and haemoptysis ceased by September 30. Nystagmus was first absent on September 26. The blood Wassermann and Kahn reactions were both strongly positive on September 24 (the G.C.F.T. was not done). Blood culture was sterile, and the C.S.F. was normal. The urethral discharge and the content of the vesicles on the glans penis were sterile.

The patient was discharged on October 6. When last seen, four months after leaving hospital, his only complaint was tiredness of the eyes in the evening. There was nothing abnormal on examination. The W.R. and G.C.F.T. were negative, although the Kahn reaction was still positive.

COMMENT

The syndrome is one of cutaneous eruption, severe conjunctivitis, stomatitis, and urethritis, associated with severe malaise. The differential diagnosis includes smallpox, Reiter's syndrome, erythema multiforme, pemphigus, septicaemia with generalized eruption, and drug intoxication. Suggested causal organisms include *Treponema vincenti, Staph. aureus,* and *Str. haemolyticus.* Few cases are reported in women; the condition most commonly occurs in young men and children. The fever may persist for weeks (Stevens and Johnson, 1922; Kove, 1945) or for a few days (Murray, 1947). The positive Wassermann cannot be considered of significance in this case, in view of the negative Wassermann reactions in all other reported cases. The condition appears to be self-limiting, reaching its maximum severity in 17 days. Stanyon and Warner (1945), who collected 17 cases of severe erythema multiforme, remarked that 14 had non-bacterial pneumonia, and two of the 17 patients died.

Almost invariably the syndrome results in impaired vision or blindness due to corneal ulceration and scarring. There is some hope, however, that chemotherapy may prevent this. In cases treated with sulphonamides the few ocular lesions that persisted were slight.

The maculo-papular type of eruption may become vesicular and resolve into deep-purple and brown areas which eventually fade, sometimes with crusting or scaling. Some physicians regard the condition as a severe type of erythema multiforme which may or may not have an allergic factor. (The value of the short course of anthisan given in this case cannot be estimated.) Many others, however, regard the Stevens–Johnson syndrome as a specific disease.

I wish to thank Dr. Wolstencroft, under whose care the patient was admitted, for permission to publish the case and for his advice: Dr. Matthews for his pathological investigations; and Mr. Gardiner for his advice on the ocular manifestations. I also wish to thank Dr. Karron, superintendent of Shrodells Hospital, Watford, for letting me read his notes on a similar unpublished case occurring in his hospital a year previously.

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Enteritis Necroticans

The following seems to be a true case of enteritis necroticans, though bacteriological confirmation was not obtained at the time. I was not then aware of the existence of *Clostridium welchii* type F enteritis, but since reading the papers by Zeissler and Rassfeld-Sternberg (1949) and Fick and Wolken (1949) I am sure my patient was suffering from this condition.

CASE REPORT

A clerk aged 61 was admitted to hospital on October 21, 1948, with vomiting, haematemesis, and melaena of 10 days' duration. A fortnight before admission he noticed swelling of the ankles and a rash in the same situation. One week previously he had had a generalized eruption, which from his description seemed to be urticarial.

On examination he was afebrile and appeared ill. There was slight oedema at the ankles, purpura was found on the ankles, elbows, and the buttocks; the abdomen was slightly distended; there was moderate albuminuria and gross melaena with flecks of fresh blood.

The white blood cells numbered 28,500; blood urea was 71 mg. per 100 ml.; the urine contained albumin, 0.5%, and a moderate number of red and white cells and casts. A culture of the stools grew *Bact. coli* and enterococci; no anaerobic culture was made. The haemoglobin was then 110%.

The patient's condition steadily deteriorated in hospital. The rash became more extensive on the buttocks, and the vomiting continued. A week after admission the white cell count was 24,300, and the haemoglobin had fallen to 90%. Nine days after entering hospital he died, following the onset of bronchopneumonia, which was treated with penicillin. Intravenous saline had been given for three days before death.

Necropsy.—The lower end of the oesophagus contained a few small haemorrhagic ulcers. The stomach showed gastritis and purpura; the duodenum, jejunum, and ileum presented diffuse haemorrhagic inflammation, with irregular areas of ulceration. These ulcers did not penetrate the muscular layers, and varied in size up to 2 by 1 in. (5 by 2.5 cm.). This condition was maximal in the distal duodenum and the upper jejunum. In the caecum, ascending colon, and transverse colon were scattered small ulcers and large diffuse areas of inflammation. A few ulcers were present in the descending colon. The lungs showed bronchopneumonia.

I am grateful to Dr. M. S. Purvis, under whose care the patient was treated, for much assistance, as well as for permission to publish this case; and to Dr. J. L. Patterson for the pathological investigations.

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Reviews

THE ORIGINS OF GENIUS

Mr. Carlyle My Patient. By James L. Halliday. (Pp. 227. 15s.) London: William Heinemann Medical Books. 1949.

The Life and Works of Edgar Allan Poe. A Psycho-Analytic Interpretation. By Marie Bonaparte. Foreword by Sigmund Freud; translated by John Rodker. (Pp. 749; illustrated. £1 15s.) London: Imago Publishing Company. 1949.

Both Carlyle and Poe might well have been included in Dr. Russell Brain's long list of psychopathic authors (December 24, 1949, p. 1427.) As Russell Brain implied in his admirable essay, there are two problems involved. The first, to establish statistically and by examination of individual histories that there is an association between psychopathology and authorship; and the second, to determine its nature. Both tasks are beset with difficulty.

If we examine the behaviour of authors it is soon realized that not only have we no adequate yardstick for normality, but that artists, unlike the rest of us, are specialists in self-expression, and their personalities, in defect and in virtue, appear to us as rather more than life-size. Because their art is an expression of themselves, conceived and executed in solitude but assessed in public, is it surprising that criticism or neglect should be felt as an attack on their ego? And that vanity, sensitivity, and flamboyance should be developed in them to an abnormal degree? If we examine their work for evidence of abnormality, difficulties appear again. Since their writing is the expression of themselves, unconscious impulses will necessarily appear in it. If there was, for example, an overt Hitler in the denunciations of Carlyle and a latent butcher of Buchenwald in the stories of Poe, is not the lesson of the twentieth century that such beasts lie, sleeping we may hope, in us all?

Dr. Halliday and Marie Bonaparte convincingly establish an abnormal personality for their chosen authors, Thomas Carlyle and Edgar Allan Poe. They do not sit in judgment on their subjects nor do they seek to explain their genius (knowing well how far we are from understanding the constitutional factors involved). But as Freud wrote in his introduction to the work on Poe, such analyses "do reveal the factors which awaken their genius and the sort of subject matter it is destined to choose." May not the same thwarting and distorting factors which in childhood produced their psychoneurosis have given these authors not only an impulse to achievement but also determined its direction?

Dr. Halliday has taught a generation of physicians here and in America to believe what they do not see and to accept what they cannot understand. In *Mr. Carlyle My Patient* he tells the life-story of Thomas Carlyle, the dyspeptic Victorian prophet who was "gey ill to live with," and in it he preaches the whole Freudian gospel—unconscious motivation, symbolism, Oedipus situation, oral, anal, and genital phases, and the rest. The psychosomatic study of Thomas Carlyle is nevertheless a brilliant narrative which well displays Halliday's skill in constructive hypothesis and ingenious analysis. No one understands human personality better than he, and no physician now writing handles words with a facility equal to his. Yet it is to be hoped that this book will not initiate a fashion in psycho-biography. A tree is better known by its fruits than by its roots, and analytical psychology is preoccupied with the morbid and irrational roots of mankind. While such studies are well justified in the interpretation of the origins of genius they do not constitute a complete and three-dimensional portrait. We need to know the height and breadth and width of a man and not his depth alone. And Dr. Halliday's picture, accurate and authoritative though it is, misses something of the strength and sweetness of Carlyle, and displays little of Jane's wit and intelligence.

One of the prime values of psycho-analytical writing is that it stimulates the critical faculty, and this is true of *Mr. Carlyle.* Not everyone will agree with the extensive use of the unconscious motive and of symbolism in the interpretation of Carlyle's thought. Halliday does not regard Carlyle's revolt against religion as a rational act. but as the result of early aggression against his mother, "who taught him the story of Jesus." When the man Carlyle remembered that as a child of 5 he asked his father "what these little black things were that I seemed to create by rubbing the palms of my hands together . . . that I described them 'like penny rolls but far less,'" these "little black things" for Halliday became "possibly the equivalent of the precious faeces which his mother had treated so ruthlessly." Or (in a footnote), "they could be regarded as the offspring resulting from his impregnation during the preceding mystic but also passively homosexual union with the father." This is a notable example of the common tendency in psycho-analytical interpretation to back at least two entirely different horses, neither of which appears likely to the sceptical onlooker to be led in by the owner The objection here is not that the mind of a child is incapable of such recondite symbolism, but simply that there is no evidence that the mind of Tom Carlyle was working in this way.

The living demand treatment and must needs suffer our diagnostic investigations; the dead ask for no therapy yet cannot escape our diagnosis. So Halliday makes no attempt to deal with certain important and inevitable questions—Could psychotherapy have "cured" Carlyle? If his psychoneurosis had been removed would his creative impulse have disappeared and what would have been his achievement?

Halliday's book is essentially for the reader who is interested in human personality, and deserves to be carefully and widely read, but Marie Bonaparte's work can appeal only to the specialist, either in psycho-analysis or in literature. The first 200 pages are biographical and interesting enough, but 500 pages are then allotted to a detailed analysis of Poe's stories. For such an interpretation of art life itself is too short. Both these books make a valuable contribution to the growing conception that there is a dynamic association between unconscious emotion and literary creation.

D. V. HUBBLE.

ESSENTIALS OF RADIOLOGY

X-ray Diagnosis for Clinical Students and Practitioners. By G. Simon, M.D., B.Ch.(Cantab.). (Pp. 207; 180 illustrations. £1.) Cambridge: W. Heffer and Sons. 1949.

Dr. George Simon, who set out to write a manual for medical students and recently qualified general practitioners, presents his survey of the subject in 200 pages and 180 illustrations, and so achieves his purpose in a readable book of modest size. It is a straightforward elementary manual of *x*-ray diagnosis, with in addition the clinical points important in *x*-ray investigation. A valuable feature is his assessment of the value and limitations of the *x*-ray method in the different diseases he describes.

The book (in which a team of clinical colleagues from St. Bartholomew's has collaborated) begins with an introduction to diagnostic radiology, in which the technology

of the subject is described in simple terms. There follow sections on the radiology of bone and joint diseases, the abdomen, the chest, and the head and neck.

When one radiologist reviews the writings of another it is inevitable for the reviewer to find points of technical disagreement. I am glad to record that I found few in this book, and I mention them with a compliment in mind—that an early second edition will soon be in demand, in which they might be reconsidered.

The author withholds magnesium salts for three days before a barium meal examination. This is surely a needless hardship to the patient. Magnesium carbonate in the colon could hardly obscure a peptic ulcer filled with barium. Again, the giving of ½–1 oz. (15–30 g.) of magnesium sulphate to fill an appendix during a barium meal is likely to cause unnecessary discomfort to the patient. One drachm (4 g.) is a more reasonable dose, and quite effective. The use of the term "dye" to describe colourless contrast media is to be deprecated. The original tetraiodo-phenolphthalein was a blue dye, but none of the other biliary or urinary contrast media is coloured. "Decalcification" of bone is referred to throughout the book, despite the fact that bone does not decalcify in any pathological process—it becomes porous by osteoclastic removal of bone, not calcium alone, as the term implies.

In the description of Paget's disease mention should be made of the sclerotic stage, and of the porotic stage in the skull. Discussing carcinoma of the colon, Dr. Simon recommends that in cases of doubt the patient should be re-examined in three months' time: a lot can happen to a cancer in three months. The discussion on the place of radiology in pulmonary tuberculosis is a well-balanced assessment of the subject, as one would expect from an author so well versed in this branch of radiology. If in a second edition he is pressed for space, he might without loss to the value of the book omit the relatively lengthy description of cardiac mensuration, catheterization, and kymography, and expand the account of the *x*-ray signs of mitral stenosis. These minor criticisms should not obscure the qualities of this excellent manual, well designed for its purpose, and one for which I predict a big demand from medical students and general practitioners. I commend it to them.

S. COCHRANE SHANKS.

MORPHOLOGY OF THE ADRENAL

The Mammalian Adrenal Gland. By Geoffrey H. Bourne. (Pp. 256; illustrated. £1 10s.) Oxford: At the Clarendon Press. 1949.

Of the many branches of endocrinology none is growing more rapidly than the study of the adrenal gland. Recent work on the part the adrenal plays in the body's response to stress and the sensational reports of its influence on rheumatoid arthritis have stimulated considerable interest. Many steroid substances can be isolated chemically from the adrenal cortex, and it is those compounds with an oxygen atom attached to the 11-carbon atom, in particular Kendall's Compound E (now named cortisone), that seem to be particularly concerned. Intensive work is being carried out also on the biological properties of the trophic pituitary hormone which controls the cortical hormone secretion, and on possible methods of synthesizing this polypeptide.

The organ has been the subject of several not very up-to-date monographs, most of which have been concerned with its clinical relations. Despite its very general title, Dr. Bourne's present book is not the general survey that is especially needed at this time. Indeed, the absence of a comprehensive analysis of the recent histochemical and experimental work on the function of the gland means that the book can have only a restricted value.

This monograph is primarily a record of work done some fifteen years ago on the comparative morphology of the mammalian adrenal. Dr. Bourne opens with a historical summary and a year-by-year survey of significant work up to 1940. He surprisingly considers that he has then succeeded in showing how our knowledge of the gland has developed, though in the same sentence he says that a large number of papers have appeared in more recent years. The rest of the book mostly consists of a species-by-species description of the morphology and microscopic appearance of the adrenals. Many of the observations, particularly on Australian mammals, are original, but are often based on scanty material. The monograph ends with a summary which, in emphasizing the constancy of adrenal structure in mammals, leads to the final conclusion that an adrenal made up of a medulla separated from, and almost completely surrounded by, the cortex is as diagnostic of the Mammalia as hair and nails.

One of the main purposes of a monograph such as this should be to provide a complete and reliable collection of references. It is therefore unfortunate that some of the authors referred to in the text do not appear in the bibliography. The illustrations are also of poor quality.

P. L. KROHN.

CARE OF THE PARALYSED BLADDER

Urological Aspects of Spinal Cord Injuries. By George C. Prather, M.D. (Pp. 146; illustrated. £1 7s.) Oxford: Blackwell Scientific Publications. 1949.

Urologists who had the responsibility during the war of looking after sufferers from traumatic lesions of the spinal cord will agree that this is far from an easy task. In no other work is a nicer judgment required, and with no other lesion is a more scrupulous care needed if grave urological complications are to be avoided. And it is upon the surgeon's judgment, care, and patience, rather than on operative skill, that the safety of the patient with a paralysed bladder depends.

In this monograph Dr. Prather reviews everything that can be considered of any importance in the urological treatment of patients suffering from injuries of the cord. He starts with an anatomical account of the bladder and its nerve supply, and then describes the pathological changes likely to occur in the genito-urinary tract after spinal injury. He concludes with a discussion of the treatment used in the various special military hospitals, American and British, in which spinal injury cases were segregated during the recent war. His survey of the neurogenic bladder is a complete one, and in no other book has so much useful information been presented in simple form.

It is gratifying to know that, in spite of the inability of the surgeon to deal directly with the primary lesion in the cord, the mortality rate has been markedly reduced by better treatment of the urinary tract. Thomson-Walker reported that over 47% of such patients arriving at the King George Military Hospital during 1915 and 1916 died within eight weeks. His condemnation of intermittent catheterization has led to the saving of many lives, and this, together with the institution of such modern methods as tidal drainage, resulted in a big reduction of mortality and a much quicker recovery in the last war. Dr. Prather has provided us with a clear account of the paralysed bladder and its care, in a book that is very easy to read and is not overloaded with statistics.

KENNETH WALKER.

INTRODUCTION TO HEREDITY

Principles of Human Genetics. By Curt Stern. Illustrations by Aloha M. Hannah. (Pp. 617; 198 figures. $5.50.) San Francisco: W. H. Freeman and Co.

Human heredity is a vast and complex subject which has been growing rapidly in recent years. In his new textbook Professor Stern approaches the subject from the standpoint of the animal geneticist rather than that of the clinician, but his perspective is admirably wide. The introduction is perhaps a little too disparaging to those who use the human race as an object of genetical investigations, as there are special advantages in studying a "wild" population as opposed to a laboratory stock.

The book gives an excellent account of the biological and cytological basis for the modern interpretation of human genetical data. No attempt is made to give clinical details or to discuss the pathology of hereditary disease. In spite of this, the book gives a fuller and better balanced account of the subject than any previous one, and includes many recent theories. The discussion on mutation and its relation to natural selection is particularly useful.

The only serious defect of the work is the paucity of reference to the methods of analysis of metrical characters initiated by Galton and Karl Pearson. In practice, almost all human traits, whether hereditary or not, are found to show gradations. This is particularly noticeable with common diseases, defects, and diatheses, which are of importance in medicine but not so interesting to animal geneticists. The medical geneticist needs more guidance in studying the heredity of metabolic abnormalities than he will obtain in the chapter on gene action, which contains several errors.

The subject of human diversity, including racial differences, is discussed learnedly and skilfully. Professor Stern describes differential fertility also, but is cautious in his treatment of eugenic problems. This is a book which can be recommended with little reservation for those who wish to base their ideas about human heredity upon a secure foundation.

L. S. PENROSE.

The Common Form of Joint Dysfunction, by William Kaufman (pp. 208; illustrated; no price; Brattleboro, Vermont, U.S.A.: E. L. Hildreth, 1949), evaluates the use of niacinamide (nico inamide) in the treatment of the "common form of joint dysfunction," which is defined by the author as impairment of joint movement due to deficiency of niacinamide in the tissues. It may be associated with other signs of "aniacinamidosis" such as changes in the skin or lingual mucous membrane, and tenderness of periosteum, cartilage, or muscle. Joint dysfunction may be present in persons who have no symptoms, or it may be associated with obvious arthritis of rheumatoid or degenerative type. From a clinical study of 455 patients Dr. Kaufman claims that the administration of niacinamide in adequate doses will lead to improvement in the range of joint movement, whether or not the impairment is associated with clinically obvious arthritic changes. To account for this improvement he presents the hypothesis that niacinamide possesses a reparative influence upon the articular cartilage of joints which balances the deteriorative factors of wear and tear and of disease. It may be argued that it is of little practical significance whether the administration of niacinamide will increase the range of joint movement in a person who is unaware of any disability from his joints. The significant question is whether the claim that niacinamide is capable of producing material improvement in rheumatoid arthritis and osteoarthritis can be substantiated. Any treatment that claims to alleviate these crippling conditions demands serious consideration. Nevertheless the evidence presented—which is based entirely on a clinical study of private patients, for the most part without radiographic study—is unlikely to arouse sustained enthusiasm unless it can be supported by controlled research, with full laboratory and radiographic investigations, in large groups of patients with typical forms of organic arthritis. This book may be of some interest to the research worker, but it will have little appeal to the clinical practitioner in Great Britain.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Electrotherapy and Light Therapy. By R. Kovács, M.D. 6th ed. (Pp. 739. 70s.) London: Henry Kimpton. 1949.

Differential Diagnosis of Chest Diseases. By J. J Singer, M.D., F.A.C.P. (Pp. 344. 52s. 6d.) London: Henry Kimpton. 1949.

Backward Children in the Making. By C. S. Segal. Introductory Note by Sir Cyril Burt. (Pp. 172. 7s. 6d.) London: Frederick Muller. 1949.

Life and Growth. By C. M. Legge and F. F. Rigby. (Pp. 79. 6s.) London: Faber. 1949.

Hospital Administration for Women. By E. Macmanus. 2nd ed. (Pp. 349. 35s.) London: Faber. 1949.

Atlas of Obstetric Technic. By P. Titus, M.D. 2nd ed. (Pp. 197. 52s. 6d.) London: Henry Kimpton. 1949.

Tuberculosis in the Commonwealth. (Pp. 411. 15s.) London: National Association for the Prevention of Tuberculosis. 1949.

The Pathology of Articular and Spinal Diseases. By D. H. Collins, O.B.E., M.D. (Pp. 331. 35s.) London: Edward Arnold. 1949.

An Atlas of Amputations. By D. B. Slocum, M.D., M.S. (Pp. 562. 140s.) London: Henry Kimpton. 1949.

Penicillin: Its Practical Application. Edited by Sir A. Fleming, F.R.C.P., F.R.S. 2nd ed. (Pp. 491. 30s., postage 1s. 3d.) London: Butterworth. 1950.

Biological Actions of Sex Hormones. By H. Burrows, C.B.E., F.R.C.S. 2nd ed. (Pp. 615. 42s.) Cambridge: The University Press. 1949.

Diseases of the Heart. By C. K. Friedberg, M.D. (Pp. 1,081. 57s. 6d.) Philadelphia and London: Saunders. 1949.

An Atlas of the Blood and Bone Marrow. By R. P. Custer, M.D. (Pp. 321. 75s.) Philadelphia and London: Saunders. 1949.

Mitchell's Pediatrics and Pediatric Nursing. By R. A. Lyon, M.D., and E. M. Wallinger, B.S. Chapter on Preventive Pediatrics by R. M. Gazeway, B.S. 3rd ed. (Pp. 590. 19s.) London and Philadelphia: Saunders. 1949.

Clinical Instruction. By A. F. Brown, B.Ed. (Pp. 571. 27s. 6d.) London and Philadelphia: Saunders. 1949.

Osler as a Gastroenterologist. By F. Cunha, M.D. (Pp. 57. 25s.) San Francisco: Felix Cunha. 1949.

Coagulation, Thrombosis, and Dicumarol. By S. Shapiro, M.D., and M. Weiner, M.S., M.D. Vol. 2. (Pp. 131. $5.50.) New York: Brooklyn Medical Press. 1949.

Vade-Mecum de Thérapeutique Infantile. By G. Mouriquand and D. Dechavanne. (Pp. 537. 1,300 francs.) Paris: Vigot. 1949

Le Guide du Médecin hors de France. Vols. 1 and 2. By J. Trabaud. (Pp. 793. No price.) Paris: Vigot. 1947

Guide Pratique de la Laborantine. By J. Marliangeas. 2nd ed. (Pp. 135. 360 francs.) Paris: Vigot. 1949.

Errori ed Insuccessi in Chirurgia Renale. By E. Cominelli. (Pp. 138. No price.) Naples: Edizioni Scientifiche Italiane. 1949.

Errori ed Insuccessi in Chirurgia Renale. By R. Ascoli. (Pp. 207. L. 1,200.) Turin: Edizioni Minerva Medica. 1949.

Medizinische Chemie. By F. Vering. (Pp. 493. Sch. 150.) Vienna: Wilhelm Maudrich. 1950

Aktive Entspannungsbehandlung. By J. Faust. 4th ed. (Pp. 127. M. 6.80.) Stuttgart: Marquardt. 1949.

Die Ausgestaltung der Organismen: Ein Chemisches Problem. By K. Noack. (Pp. 38. M. 2.50.) Berlin: Akademie. 1949.

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PROGNOSIS IN PERFORATED PEPTIC ULCER

Operations on patients with perforated peptic ulcer qualified from the very first for inclusion in what Gordon-Taylor has called the dramatic in surgery. Each early success meant that a patient had been saved from almost certain death. In such circumstances the value of an operation is apt to be judged by the recovery rate and not by its mortality rate. Thus operation soon became recognized as the correct treatment for a perforation, though the risks must have been considerable. Even in the years between the wars, when standards of surgical skill, anaesthetic technique, and post-operative care were by no means low, the mortality rate in the best hands was about 25% and in many places was well over 30%. With the impetus which the second world war gave to emergency abdominal surgery and to resuscitation, and with the advent of sulphonamides, penicillin, and curare, a considerable drop in mortality was to be expected. As recently as 1946, however, it was stated in these columns, "A mortality of below 10% is satisfactory in the present conditions."[1]

The persistence of this hard core of fatal cases was thought to be due to late operation; for it was shown that the risk of death was greatly increased when surgery had to be undertaken eight or more hours after perforation. That this was only a half-truth is demonstrated by Dr. F. Avery Jones, Dr. P. J. Parsons, and Miss Barbara White in a paper which appears elsewhere in this issue. This is a careful analysis of nearly five hundred cases of perforated peptic ulcer treated at the Central Middlesex Hospital between 1938 and 1948, inclusive. During this period the mortality rate has been reduced from 27% to only 4%, despite an increase in the number of older patients, with no change in the proportion of late cases, and with an actual increase in the number of patients who were moribund on admission. The reduction in the number of deaths occurring in the immediate post-operative period is a remarkable improvement: since 1943 there have been no deaths from perforated gastric ulcers in the week following operation. There have been four such deaths from duodenal ulcers, but if the mortality rate of 1938–42 had remained unchanged the number of deaths to be expected would have been 29. When the cases admitted during 1938–40 are compared with those admitted during 1947–8 it can be seen that post-operative shock and peritonitis have been virtually abolished; acute chest complications—basal collapse and infections—occur just as often, but respond to treatment; late chest conditions—lung abscess and empyema—have disappeared; and subphrenic abscesses and wound infections are much reduced. Haemorrhage still occurs and presents special problems of its own.

The routine use of sulphonamides and penicillin and the introduction of cyclopropane anaesthesia and curare are probably responsible for these gratifying improvements. The importance of the first two, and of the sulphonamides in particular, is clearly shown by Dr. Avery Jones and his colleagues. Before 1943, the first year in which sulphonamides were used on a large scale, the average mortality from acute perforation was 25%; but in that year it fell to 6%. Most would agree with the statement that it is probable that sulphonamides and penicillin have played a larger part than the new anaesthetic techniques. Indeed, the unchanged incidence of acute respiratory complications still offers a challenge to anaesthetists in these cases. It is understandable that in a paper by physicians surgical details are scanty, but the authors emphasize the importance of ensuring that at the end of the operation no fluid is left above the liver. Nevertheless, though the surgeons may obtain most gratification from the excellent results, in one respect the physicians concerned have done themselves less than justice. Dr. Avery Jones and his colleagues suggest that the post-operative care which these patients received in the medical wards merely increased their comfort and did not contribute a great deal towards the lowered mortality. This may be so, and the infrequency with which resuscitation with blood transfusion was required does suggest that the surgery was of a very high standard. But the remarks made about post-operative management merit very close study by all who have to treat these patients: the electrolyte balance must be maintained, and for this purpose the authors demonstrate the value of the rectal administration of fluid. In this connexion it is perhaps not sufficiently realized that patients can easily be given too much saline solution intravenously. But even when the surgical skill is of the highest, the anaesthetic given with greatest proficiency, and the post-operative supervision most careful, a few patients die after operation for perforated peptic ulcer. A difficulty still to be overcome is the occurrence of haematemesis or melaena during convalescence. The question of the prevention of this complication by a more radical procedure than simple suture at the time of operation remains to be considered. Relevant to this problem are the observations of Dr. Richard Doll, whose paper drawing attention to the

[1] *British Medical Journal*, 1946, **2**, 950.

frequency with which perforation occurs in carcinoma of the stomach also appears in this issue. In a series of male patients 8% of 86 cases diagnosed as simple gastric ulcer at the time of perforation proved to be malignant within three years.

POLIOMYELITIS AND THE COXSACKIE VIRUS

In 1947 Dalldorf and his collaborators,[1 2] while investigating cases of apparent poliomyelitis which were then occurring in New York State, isolated a virus having properties different from any hitherto described. In attempting to isolate the poliomyelitis virus it is usual to obtain specimens of faeces from the patient: a suspension of the faeces is treated with ether to kill bacteria and then injected intracerebrally into monkeys. If the animals become paralysed the virus may be readily obtained from the central nervous system and propagated indefinitely in monkeys. A small proportion of the strains of poliomyelitis virus isolated in this way can be adapted subsequently to multiply in cotton rats or in mice by intracerebral passage: the best-known examples of these strains are the Lansing and the Y-SK. Early in 1947 Milzer and Byrd[3] had reported that primary isolation of some poliomyelitis strains might be possible in mice provided that the ether-treated stool suspension was mixed with autolysed brain tissue before being injected intracerebrally, and Dalldorf had been trying this new technique, but without success. However, he also injected the specimens intracerebrally into suckling mice, because laboratory tests with other neurotropic viruses had suggested that very young mice were more susceptible than adult mice. Suckling mice injected with faeces from two patients became paralysed in from 5 to 11 days and died. It was soon found that simultaneous injection of autolysed brain tissue was unimportant but that the age of the mouse was crucial. Newborn mice or mice not more than four or five days old proved the best; it was not possible to infect mice more than 12 days old. After passage a few times through suckling mice the virus, injected either by the intracerebral or by the intraperitoneal route, killed the mice in three days. The strains isolated from both patients appeared to be the same. Although the virus was present in high titre in the central nervous system of the mice there were no microscopical lesions such as are caused by the poliomyelitis virus. The paralysis was due to a widespread myositis with subsequent hyaline degeneration, and the virus was found to be concentrated about 10.000 times more strongly in the muscles than elsewhere.[4]

Clearly the new virus was no ordinary strain of poliomyelitis virus; moreover, monkeys could not be infected by it, though it would infect suckling hamsters and newborn guinea-pigs. The specimens of faeces containing the virus were examined for strains of poliomyelitis virus by intracerebral injection into monkeys, but none were found. The two patients from whom the new virus was isolated lived in the village of Coxsackie (in New York State), which at that time had five other cases of apparent poliomyelitis. Both patients had paralysis of the lower limbs from which they took many months to recover: neutralizing antibodies for the new virus appeared in the blood of both patients during convalescence. Ten contacts of these cases were examined for serological evidence of infection with the same virus. Five of these had neutralizing antibodies in their sera, but since there was no information about the presence of such antibodies in the general population it is difficult to be sure that there had been recent infection. In 1948 nine more strains of the Coxsackie or "C" virus were isolated from apparent cases of poliomyelitis in New York State; two of the patients were paralysed. Five more strains were isolated during an epidemic in central Wilmington, and at the same time Melnick isolated typical strains of poliomyelitis virus from cases occurring in the suburbs of Wilmington. Thus it appeared that two different epidemics were occurring at the same time in the same place.

Later in 1948 there were epidemics of what appeared to be poliomyelitis in Connecticut and in Rhode Island, and Melnick and his collaborators[5 6] collected specimens of faeces from representative cases and stored them at −70° C. pending investigation. The cases were classified into paralytic and non-paralytic, the latter including some which had been diagnosed as aseptic meningitis in order to avoid using the ominous word poliomyelitis. It was observed that the paralytic and the non-paralytic cases were distributed differently in time, suggesting that as in the Wilmington epidemics two different viruses might be responsible. Specimens of faeces from 14 of the non-paralytic cases were inoculated into suckling mice, and from five of them a virus similar to the Coxsackie virus was isolated. The specimens of faeces were also injected intracerebrally into monkeys, and from two of those which did not contain a Coxsackie virus strains of poliomyelitis virus were isolated. All five of the patients excreting the Coxsackie virus had neutralizing antibodies for it in their sera, and in five of the patients with non-paralytic poliomyelitis from whom no virus could be isolated neutralizing antibodies for the new virus were demonstrated. In only one case, however, was it possible to show an actual rise in these antibodies.

[1] *Science*, 1948, **108**, 61.
[2] *J. exper. Med.*, 1949, **89**, 567.
[3] *Science*, 1947, **105**, 70.
[4] Gifford, R., and Dalldorf, G., *Proc. Soc. exp. Biol., N.Y.*, 1949, **71**, 589.
[5] *Ibid.*, 1949, **71**, 344.
[6] *J. Amer. med. Ass.*, 1949, **141**, 894.
[7] Sickles, G. M., and Dalldorf, G., *Proc. Soc. exp. Biol. N.Y.*, 1949, **72**, 30.
[8] Sabin, A. B., and Steigman, A. J., *Amer. J. Hyg.*, 1949, **49**, 176.

The evidence which is accumulating suggests that there are at least three antigenic types of the Coxsackie virus,[7] and a complement-fixation test has been devised for the elucidation of the problem. The size of the virus is uncertain: it is one of the smaller viruses, but it is probably somewhat larger than the poliomyelitis virus. It has been isolated from sewage and from flies, but it does not appear to be ubiquitous, for many adult human sera do not neutralize it. In contrast, in New York State only sera from the very young fail to neutralize the Lansing strain of poliomyelitis virus. The Coxsackie virus has been isolated from a patient who at the same time was excreting a strain of poliomyelitis virus, though in this case serological evidence suggests that it was the Coxsackie virus which was responsible for the patient's illness. There are wide variations in the severity of the illness caused by the poliomyelitis virus; some infections are completely asymptomatic and demonstrable only by finding virus in the intestinal tract, and cases of non-paralytic poliomyelitis occur which may simulate a trivial gastro-intestinal upset. The strains of poliomyelitis virus themselves differ in virulence, so that some may cause epidemics in which there are very few cases of paralysis and the epidemic as a whole is referred to as a "summer grippe."[8] The new Coxsackie virus seems to cause epidemics of this latter type, but is also associated with epidemics of true poliomyelitis. It is reasonable to suppose that when the patients infected with the new virus are paralysed, the paralysis is due not to injury of the central nervous system but to involvement of the muscles. However, this supposition is at present based only on the behaviour of the virus in suckling mice. Patients dying of true paralytic poliomyelitis may also have muscle lesions, and this serves to emphasize the close relation between the new virus and the poliomyelitis virus. In addition to simulating poliomyelitis the new virus may be the cause of some cases of epidemic myalgia. In the three laboratory infections which have occurred the patients' main symptoms were abdominal and thoracic pains, and the virus has been isolated from a case diagnosed as epidemic pleurodynia.

THE ADAPTATION SYNDROME

A few weeks ago we published a paper by Professor Hans Selye[1] in which he described experiments demonstrating the influence of the pituitary-adrenocortical system on the production and prevention of experimental arthritis. He discusses in a paper appearing in this issue further work on the pathogenesis of "diseases of adaptation." As a result of experimental work on animals Selye has suggested that following exposure to stress—a term used to include such diverse conditions as emotional tension, infections, and intoxications—the body responds by increased production of hormones from the adrenal cortex.[2 3] These hormones help to raise the general resistance of the body to the stress to which it is subjected. Selye maintains that this adaptive mechanism may itself become deranged, and he has produced in animals a variety of conditions which are perhaps the experimental counterparts of rheumatoid arthritis, rheumatic fever, nephrosclerosis and hypertension, and periarteritis nodosa. The adrenal cortical hormones may be broadly divided into two main groups —the gluco-corticoids (such as corticosterone and cortisone) and the mineralo-corticoids (such as desoxycorticosterone or DCA). The two groups differ in their effect on the organism. In experimental animals Selye[4] found that corticosterone increased, whereas desoxycorticosterone diminished, the resistance to traumatic shock. Overdosage with desoxycorticosterone itself may induce the conditions mentioned above, especially if the animal has previously undergone unilateral nephrectomy and is given a diet with a high salt content. It is suggested, therefore, that stress causes the adrenals to liberate cortical hormones, and if there is disproportionate overproduction of the mineralo-corticoids the diseases of adaptation may appear.

Two main objections have been raised to this experimental work. First, contrary to widespread belief, there is little evidence that desoxycorticosterone is a naturally occurring substance or that it is secreted by the adrenal cortex. It has only once been isolated from the suprarenal glands,[5] and this may well have been an artifact produced in the laboratory. Secondly, since desoxycorticosterone does not occur naturally, the reactions it provokes may be the allergic responses of the body to a foreign substance. Professor Selye now reports some observations which go far towards dispelling these objections. A naturally occurring mineralo-corticoid, 11-desoxocortisone, has been injected into rats which have been "conditioned" by a unilateral nephrectomy and the administration of excess sodium. The lesions produced (nephrosclerosis, hypertension, periarteritis nodosa, and granulomatous nodules in the heart) are similar to those seen after overdosage with desoxycorticosterone.

It remains to be seen how the results of these experiments on rats with one kidney removed, given much salt, and injected with large doses of mineralo-corticoid hormone can be compared with diseases in man. Selye[6] has shown in animals that a gluco-corticoid (cortisone)

[1] *British Medical Journal*, 1949, **2**, 1129. See also leading article on p. 1159
[2] *J. clin. Endocrinol.*, 1946, **6**, 117.
[3] *Practitioner*, 1949, **163**, 393.
[4] *Canad. med. Ass. J.*, 1940, **43**, 1.
[5] *Helv. chim. Acta*, 1938, **21**, 1197.
[6] *Canad. med. Ass. J.*, 1949, **61**, 553.
[7] Hench, P. S., Kendall, E. C., Slocum, C. H., and Polley, H. P., *Proc. Mayo Clin.*, 1949, **24**, 181.
[8] Thorn, G. W., *et al.*, *New Engl. J. Med.*, 1949, **241**, 529.
[9] Hench, P. S., *et al.*, *Proc. Mayo Clin.*, 1949, **24**, 277.
[10] McNee, J. W., *British Medical Journal*, 1950, **1**, 113.
[11] *Practitioner*, 1949, **163**, 365.
[12] *Lancet*, 1950, **1**, 116.

will inhibit the development of adaptation diseases which can be induced by desoxycorticosterone. Similarly it has been shown in man that cortisone will relieve the symptoms not only of rheumatoid arthritis[7] but also of rheumatic fever, chorea, gout, ulcerative colitis, lupus erythematosis diffusa, scleroderma, and asthma.[8 9 10] It is tempting in the absence of any known cause for these conditions to suppose that they are the products of disordered adaptation, but as yet there is little evidence for such an assumption. It is unlikely that treatment with cortisone is merely replacement therapy: Thorn and Bayles[11] have pointed out that, whereas 10–20 mg. of cortisone daily will maintain a patient with complete adrenal insufficiency, 100 mg. a day may be required to change the course of rheumatic disease. If, then, it is a question of imbalance between gluco- and mineralocorticoids, either the presence of excess mineralocorticoids—which might block the "target organs," so that cortisone cannot act upon the affected tissues—or some general disturbance of steroid metabolism must be demonstrated. Recently Marrian and his colleagues[12] have shown that at least one steroid (progesterone) is not metabolized normally in patients with rheumatoid arthritis, but whether there is a similar defect in the metabolism of cortisone is as yet unknown. Finally it should not be forgotten that although several pure steroids have been isolated from the adrenal cortex none is as active weight for weight as the amorphous fraction, the composition of which still awaits elucidation.

RADIOLOGICAL DIAGNOSIS OF PNEUMOCONIOSIS

The radiological diagnosis of early tuberculosis is not always easy, and it has been shown that experienced radiologists not only differ between themselves but also do not consistently repeat their original assessment when making a subsequent examination of the same films. This naturally raises the question whether the same difficulties attend the diagnosis of other chest conditions from *x*-ray films. A chest radiograph provides the only certain method of diagnosis of pneumoconiosis in life, and estimates of the progress of the disease and most schemes of classification are based on the radiological findings. Accuracy of classification is important, since on this depends compensation and the decision about the type of work for which the patient is considered fit. Fletcher and Oldham[1] recently undertook to find out for the Pneumoconiosis Research Unit of the Medical Research Council how accurately the progress of pneumoconiosis could be assessed in coal-miners who had continued to work underground for some years since they were first examined. Ten radiologists who were experienced in the early diagnosis of coal-miners' pneumoconiosis and two consultant radiologists in London classified 102 films into five categories: (1) normal; (2) very early pneumoconiosis; (3) definite pneumoconiosis, but not certifiable for purposes of compensation; (4) definite pneumoconiosis of certifiable degree, but showing only "reticulation"; (5) more than "reticulation"—i.e., "nodulation" or "coalescent shadows." The films, which were classified twice, the second time in reverse order, were selected from three sources and included over- and under-exposed films. There was much disagreement between the opinions given on each film, for of 56 films considered on at least one occasion as normal five were placed, on at least one occasion, in category 2, 17 in category 3, 21 in category 4, and 11 in category 5.

For compensation purposes the silicosis medical boards are only required to place the films above or below a certain standard of abnormality. This standard has not been rigidly defined, and the inconsistencies of opinion between different radiologists may have been due partly to the different interpretations made by them. Categories 4 and 5 in the investigation included certifiable pneumoconiosis, and Fletcher and Oldham used these groups to examine the errors of certification. There were large differences between the findings of the radiologists, and the number of cases classified as certifiable at least on one occasion ranged from 16 by one radiologist to 63 by another. The consistency of certification—the number certified in both tests as a proportion of the number certified in either test—ranged from 31% to 87%. One of the two senior members of the silicosis medical boards certified 50% more cases than his colleague. Radiographic technique was found to be a factor of importance in determining classification. Under-exposed films were generally considered to show more disease than over-exposed films of the same case taken on the same day. The results obtained in this investigation show that the certification of any applicant may depend on which particular doctor happens to assess his film and even on day-to-day variations in this particular doctor's opinion of what constitutes certifiable pneumoconiosis. Because of the importance that is necessarily attached to the radiological diagnosis of pneumoconiosis there is an urgent need of some method that will give more consistent results. Fletcher and Oldham suggest "that the present method by which films are diagnosed by simple scrutiny should be superseded by a method of comparison of unknown films with accepted standard reference films."

1 *Brit. J. industr. Med.*, 1949, 6, 168.

HOSPITAL-TREATED SICKNESS IN SCOTLAND

The Health and Sickness Records Bureau at Glasgow University has published the results of a survey in Ayrshire[1] similar to that carried out a year or two ago in the smaller county of Stirlingshire.[2] The object was to find out how much sickness was hospital-treated, either at the 18 hospitals of Ayrshire itself or in hospitals outside the county—almost invariably in Glasgow, which is only 12 miles from the county's northern tip. Ayrshire is a mixed industrial and agricultural county, with an important mining element; the population is 315,500. The standard of housing leaves much to be desired, and in the burgh of Ayr itself, which, according to its famous son, "ne'er a town surpasses for honest men and bonnie lasses," the

1 *Hospital and Community. II. Hospital-treated Sickness amongst the People of Ayrshire.* The Health and Sickness Records Bureau (Glasgow) and the Nuffield Provincial Hospitals Trust (London and Edinburgh).
2 See leading article in the *British Medical Journal*, 1948, 2, 686.

proportion of overcrowded houses is almost one-third of the total: in two of the six wards almost one-half. Hospital accommodation in Ayrshire—1,867 beds, apart from 781 in mental institutions—is sufficient for immediate needs. Rather less than one-sixth of those requiring in-patient treatment find accommodation in Glasgow, and one-twelfth of the out-patients from the county make their first attendances there. It has been ascertained that in the course of one year the actual number of individuals who received in-patient treatment, either in the county or beyond it, was 22,416, and those attending for the first time as out-patients numbered 32,089. After adjustment of the figures for those who received both out- and in-patient treatment during the year it appears that 46,660 Ayrshire residents, or one in seven of the population, received some form of hospital care.

The diseases which brought most in-patients to hospital, both men and women, were those of the digestive system, but these were on the average short-stay cases—11.6 days for men and 10.5 for women. In the next largest group, consisting of infective and parasitic diseases, patients remained, on average, over 70 days in hospital, owing chiefly to the heavy load of tuberculosis. The average duration of stay in hospital for a patient with pulmonary tuberculosis was 162 days; about 2% of the 531 cases were discharged as "cured," but 75% were "improved." Eight hundred and ninety-six patients were admitted to hospital for the treatment of neoplasms—most frequently of the digestive system in males and of the genital organs and breast in females—and in 668 cases the growth was malignant. The majority of patients with eye diseases and injuries needing in-patient treatment go to city hospitals, but 2,450 out-patients were treated at Ayrshire hospitals for eye conditions. On the other hand, only 7% of those with disease of the ear found it necessary to go outside the county. An attempt was made to assign the patients to social classes according to the classification which the Registrar-General adopted at the 1931 census. Respiratory diseases, diseases of the skin and cellular tissues, and injuries bulked most largely in classes 4 and 5. The percentage of patients treated for digestive diseases was much larger in the highest and lowest social groups than in the intermediate.

In round figures, 7,000 of the 17,000 in-patients (apart from maternity cases) were entered on the hospital records as discharged "cured" during the year; 7,500 as "improved"; 1,200 as "unchanged"; and 59 as "worse." Deaths numbered 873. But there is little value in such figures because of the wide variations in curability of the conditions for which the patients were admitted. Thus 56.6% of the persons admitted for infective and parasitic diseases (though tuberculosis was included in this category) were "cured," but only 23.9% of those admitted with neoplasms. One in three of the females who received in-patient treatment was admitted for childbirth (average stay in hospital 13.8 days) or for some complication of pregnancy. The authors of the report point out that both in Stirlingshire and Ayrshire a large proportion of patients leave hospital on completion of treatment before they fully recover their health. It is worth noting what a burden accident places upon hospitals in an area which is only partially industrial. During the year 1,633 injured or poisoned patients were admitted to hospital: 436 sustained injury at work, 252 at home, 207 at play, and 199 on the road. Fractures were the commonest injury. Out-patients attending for the first time as the result of accident numbered over 9,000.

SCOTTISH REPORT ON GENERAL PRACTICE

The Scottish Medical Practices Committee has followed its English counterpart in publishing a report of its work, which appears on another page, and in listing areas where, in its opinion, more doctors are needed. Discussing the controversial question of what should be the maximum number of patients permitted on a general practitioner's list, the committee plainly indicates that 4,000 is too high a figure. "Even in compact industrial areas such a large commitment represents a burden too heavy for the practitioner to continue to bear"; and "the maximum number of patients should be more nearly related to an optimum figure considerably lower than the present limit." Many would agree with the committee, though it must not be forgotten that as the permitted maximum is reduced so is the patient's free choice of doctor restricted. In any case satisfactory assurances would need to be obtained from the Scottish Department of Health and from the English Ministry that the Spens Report would be implemented and that general practitioners would not suffer financially if the maximum size of their lists were lowered.

Dispersal of patients when a doctor withdraws from his practice or dies causes disquiet in Scotland as it does in England, and may add greatly to the burden of the doctor starting practice. The problem is to combine speed in appointing the new practitioner with fairness to all the applicants, and it has not been solved yet. The committee reports that it has discussed the matter with the Department of Health and other bodies, and the outcome will be awaited with interest. The list of "under-doctored" areas in the appendix to the report offers guidance to general practitioners seeking openings in Scotland, and presumably the committee will follow the practice of the English M.P.C. in publishing amendments to the list as the situation changes.

ALLERGIC FACTORS IN GOUT

One well-established fact about gout is its association with a disturbance in the metabolism of uric acid which results in hyperuricaemia. The underlying metabolic defect is apparently genetically determined, probably by a single dominant autosomal gene, but, as Smyth and his colleagues[1] point out, only a small proportion of these hyperuricaemic subjects develop clinical gout. As long ago as 1911 Linossier and Leri,[2] impressed by the suddenness of the onset of the attacks, the completeness of the recovery, and the relationship to food, concluded that the arthropathy of gout was related to that of serum sickness. Three cases described by Harkavy[3] certainly indicate that allergic factors are concerned in the genesis of the acute attacks. The patients could take purine- and fat-containing foods with impunity so long as the sensitizing substances were

[1] *J. clin. Invest.*, 1948, **27**, 749.
[2] Quoted by Urbach, E., and Gottlieb, P. M., in *Allergy*, 1946. London.
[3] *J. Amer. med. Ass.*, 1949, **139**, 75.
[4] *Pr. méd.*, 1947, **55**, 882.

avoided. Two of the three had family histories of allergy, and all gave positive skin reactions to pollens and a variety of foods. Most convincing, however, was the fact that intentional exposure to the allergenic agents consistently precipitated attacks of gout. Bacterial sensitization as a result of upper respiratory infections also appeared to be an excitatory cause in two of the three patients.

The allergic stimulus is only one among many that may bring on an acute attack of gout. Other well-recognized stimuli include alcoholic beverages, excessive intake of fats, surgical and other traumata, and exposure to severe weather. It would thus appear either that the gouty diathesis renders the tissues, especially the joints, unusually susceptible to a variety of allergic or non-allergic stimuli, or that the acute attack, as in many cases of asthma, is the result of an allergic reaction and the various agents enumerated above merely serve to precipitate it. If the latter be the case the gouty diathesis may be looked upon as predisposing to attacks of acute arthropathy in two ways, by favouring the development of allergy itself and, possibly, by conducing to localization of the allergic reaction within the joint tissues. What determines the location of antigen-antibody reactions and consequently the site of the "shock organ" is one of the least understood aspects of allergy. In our present state of knowledge it might be reasonable to suppose that either the hyperuricaemia or the underlying metabolic defect may play a part in localizing such antigen-antibody reactions to the joints in general and the big toe in particular. The evidence in favour of the allergic nature of any disease is to-day incomplete without consideration of the effect of the antihistamine drugs. Owing to the wide pharmacological activity of many of these drugs conclusions must be drawn with care, but it is of interest that Violle[4] has already reported that they are of value in the therapy of acute gout.

RESUSCITATION OF THE NEWBORN—A POSSIBLE DANGER

Nikethamide and a related drug known as "cycliton" are generally considered to be harmless when used in therapeutic doses. This is certainly true in adults, but according to Drs. F. P. Hudson, A. McCandless, and A. G. O'Malley, whose paper on sciatic paralysis in newborn infants appears elsewhere in this issue, there is a definite hazard when these drugs are injected into the umbilical cord of the newborn. This is a common practice in infants suffering from asphyxia neonatorum. Hudson and his colleagues record 20 cases of unilateral sciatic paralysis, sometimes accompanied by cutaneous gangrene of the buttock on the same side, in newborn infants in the maternity departments of two Liverpool hospitals. Investigation of the possible causes disclosed that the only factor common to all the cases was the injection of cycliton into the cord for the treatment of asphyxia. The first report on this new neonatal syndrome came from Mr. W. G. Mills,[1] in Birmingham, who recorded eight similar cases after the injection of nikethamide into the cord for the treatment of asphyxia neonatorum. Bates and Page[2] have also reported a case. It is possible that the injections were given accidentally into the umbilical artery in mistake for the vein, for it is well known that the accidental intra-arterial injection of drugs, or even saline solutions, may cause prolonged arterial spasm, sometimes leading to intra-arterial thrombosis and gangrene. There have been many reports on gangrene of the arm caused by the accidental intra-arterial injection of thiopentone; this probably causes arterial spasm because of its high *p*H, which makes it extremely irritant. This explanation would not hold for arterial spasm caused by the injection of cycliton, which is only slightly acid in solution. However, both cycliton and nikethamide are used in 25% solution. Although the compounds themselves may be harmless enough pharmacologically, solutions of such a concentration might conceivably irritate the endothelium of an artery and cause arterial spasm and thrombosis. Solutions of salt only slightly stronger than this are employed as sclerosing agents. It it noteworthy that when small amounts of cycliton were injected into the umbilical arteries of newborn kittens none of the animals survived longer than twenty-four hours.

In the foetus the blood supply to the lower limb is carried by the sciatic artery, the main branch of the internal iliac; the external iliac artery provides merely a subsidiary supply. After birth the function is reversed, the main blood supply being taken over by the external iliac artery, the sciatic becoming quite small and functioning as the nutrient artery of the sciatic nerve. In asphyxia neonatorum the veins would be collapsed, and it is quite possible that an injection into the cord might be made into one of the two umbilical arteries. The fluid would pass to the hypogastric artery and to the sciatic artery via the internal iliac artery. Spasm of the smaller sciatic artery, followed by thrombosis, would greatly reduce the blood supply to the sciatic nerve and the buttocks, with resulting paralysis and gangrene. This is a possible explanation of the neonatal syndrome described by the Liverpool and Birmingham obstetricians, but proof is lacking. Obviously great care should be taken when giving injections into the cord, and it would seem wise to dilute nikethamide and similar drugs. The injection of other analeptics which are employed in more dilute solutions might also be considered.

THE LOCK HOSPITAL

At a meeting on January 9 the North-West Metropolitan Regional Hospital Board decided to abandon its plan to change the use of the London Lock Hospital. The Ministry of Health has communicated with the Board, and in the words of a statement issued recently: "It was agreed that, whilst the Board had no alternative other than to accept the Minister's decision that the proposed change of user should not be proceeded with, a reply be sent reiterating the Board's views on the matter." This *Journal* first drew attention[1] to the threatened closure of the Lock Hospital in May last year, saying that "to remove the London Lock Hospital from Dean Street would be an act of medical vandalism and disservice to a peculiar part of London's population." The people of Soho, no less than the medical profession, will welcome this intervention by the Ministry of Health.

[1] *British Medical Journal*, 1948, 2, 956; 1949, 2, 464.
[2] Ibid., 1949, 2, 756.

[1] *British Medical Journal*, 1949, 1, 948.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MEASLES

BY

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Measles is still a serious disease in this country, particularly in young children up to 2 or 3 years of age. Although its virulence has declined in a remarkable fashion in the last twenty years and deaths have fallen to a record low level, it is still capable of causing extensive and permanent damage, especially to the lungs, middle ear, and eyes. Before this decline measles probably killed more children than any single infectious condition except enteritis, and though hygiene and better nourishment have had considerable effect in controlling the disease an increase in its virulence is always possible.

Aetiology

The causative virus gains access to the body through the respiratory tract by droplet infection from another sufferer. The disease is intensely infectious, especially in its early stages, and all ages are susceptible. Young infants are immune if their mothers have had the disease, and they do not lose this maternal immunity completely until they are about nine months old, after which time unmodified measles may be expected. If the mother has not had measles her infant will be susceptible from birth.

Like most virus diseases measles has a long incubation period, of from ten to twenty-one days, twelve days being the average for an unmodified attack; the immunity produced usually lasts for life and second attacks are rare. In modified measles the incubation period may be longer.

The measles virus seems to have the property of lowering the resistance of the respiratory mucous membrane and rendering it susceptible to attack by secondary bacterial invaders, particularly the streptococcus and pneumococcus.

Clinical Features

In spite of the rash being such a prominent feature measles should be regarded as essentially a respiratory disease in which the whole respiratory tract may be involved. In the prodromal stage, which usually lasts three to four days but may be longer, the upper respiratory tract bears the brunt of the attack. The condition then simulates an acute cold, and coughing, sneezing, and lacrimation, associated with general misery, are prominent features. It may sometimes be accompanied by a catarrhal laryngitis, which is often mistaken for laryngeal diphtheria. The temperature will almost certainly be raised and a marked degree of conjunctivitis may be present.

Koplik's Spots.—A careful inspection of the mouth, an essential part of the examination of any child whatever disease is suspected, will probably reveal the presence of Koplik's spots. These spots are pathognomonic of measles and resemble grains of salt on a reddened buccal mucosa. Sometimes they are so numerous as to become confluent in places. They are usually found opposite the molars and can be seen only in good daylight or with a lamp giving proper colour values. They are practically invisible with ordinary electric light, and the small pocket torch is useless. The spots rapidly clear on the appearance of the true rash (for this reason they are usually looked for too late), though a reddened and granular appearance of the mucous membrane often persists for a short time. In addition, some degree of stomatitis is always present and the mouth may become foul.

Prodromal Rashes.—These occur occasionally and may take the form of a fine macular rash on the trunk suggesting rubella, or of a scarlatiniform eruption falsely indicating scarlet fever. The scarlatiniform type of prodromal rash is occasionally the cause of the double diagnosis of scarlet fever and measles being made. The two diseases do not usually occur together, though as previously stated the streptococcus is an early secondary invader in measles, particularly in the mouth, nose, and middle ear, and on the fifth or sixth day the patient may present a typical peeled streptococcal tongue as in scarlet fever.

Respiratory catarrh may occasionally be accompanied by appendicular catarrh and the signs of acute appendicitis. In such cases operative intervention may be necessary. I saw four examples last year, all of which came to operation.

The Rash.—The true rash of measles begins as a few fine macules behind the ears and rapidly spreads on to the face and then to the trunk and limbs, finally reaching the feet. The lesions are often papular as well as macular and coalesce to form irregular, dusky red, blotchy patches. Sometimes large areas of skin, especially on the trunk, are covered by a confluent eruption somewhat suggesting scarlet fever. On the other hand, the rash may remain macular and discrete, particularly in modified measles.

When the rash is very heavy it may contain obvious haemorrhagic elements. This is not necessarily a sign of a severe attack (true haemorrhagic measles is very rare), and in most patients with a heavy eruption staining due to altered blood pigment is left behind when the rash fades. A branny desquamation occurs also. With the appearance of the true rash the temperature, which usually falls to normal at the end of the prodromal period, rises again. In uncomplicated cases it falls in three to four days.

In ordinary cases the rash usually subsides by the end of a week; the patient rapidly becomes convalescent and may be allowed up. He may safely be regarded as free from infection by the end of ten days' illness and can be considered cured by the end of the second week.

Complications

Complications involving the respiratory tract are the most common and are generally due to secondary bacterial infection.

Otitis.—Infection may spread from the nasopharynx to cause otitis media, the most common complication of measles at the present time. It is usually suppurative, but with early treatment by chemotherapy is unlikely to be followed by mastoid disease. Deafness may occur.

Laryngitis.—Secondary laryngitis developing as the true rash fades is a much more serious condition than the early catarrhal laryngitis of the prodromal stage. It may become obstructive and is nearly always either diphtheritic

or streptococcal in origin ; it must be treated as diphtheritic until proved otherwise.

Bronchitis.—This is a common and sometimes severe complication that may be followed by bronchopneumonia, often of the interstitial variety, which is particularly likely to give rise to subsequent fibrosis and bronchiectasis. Lobar pneumonia is not a usual complication in young children, and empyema after either form of pneumonia is at present rare.

Enteritis.—This complication is most likely in infants and may be a danger to life. It may be present in the early stages as a toxic manifestation, but if it persists is probably due to secondary infection. All the classical signs of infantile gastro-enteritis may be present, with dehydration and liver damage.

Eye Lesions.—Conjunctivitis is a normal accompaniment of measles, but corneal ulceration may occur very rapidly, particularly in debilitated children, and have serious consequences. Opacities that seriously impair sight may result, and perforation of the anterior chamber and disorganization of the eye have been known to follow in the worst cases.

Encephalitis.—Post-infective encephalitis may occur in measles as in other virus diseases. It usually shows itself at the end of the first week. The damage may be minimal, but in anything up to 30% of cases it is severe enough to cause death. At least half of the cases that survive seem to make a complete recovery, but the remainder may develop epileptic fits and mental deterioration. In the early stages meningeal irritation may be present, with irritability or convulsions. Stupor or complete unconsciousness may supervene, and during the slow recovery stage spasticity of the limbs is a pronounced feature. Myelitis may coexist.

Associated Diseases.—Measles can be deadly in association with other diseases. Laryngeal diphtheria has already been mentioned, and the combination of measles and whooping-cough greatly increases the risk of severe pneumonia and subsequent fibrosis. Tuberculosis of the lungs is not so common after measles as was once thought, although it may be lit up by a bad attack of pneumonia in a previously infected subject.

Diagnosis

A history of exposure to measles should always be sought. The combination of pyrexia, catarrhal signs, and a generalized morbilliform rash is enough strongly to suggest measles, and if Koplik's spots are seen the diagnosis is established. In the prodromal stage the disease has to be distinguished from the ordinary cold, from laryngeal diphtheria, and, more rarely, from the catarrhal stage of whooping-cough. In the latter disease catarrhal signs, including laryngitis, may be pronounced. The prodromal rashes have already been mentioned as suggesting rubella or scarlet fever, but confusion with these two diseases may also occur when the true rash appears. The rash of rubella is pink, however, and the macules are smaller and usually discrete. In addition all the superficial lymph glands are enlarged, including the occipital, post-cervical, and, most typical of all, the mastoid.

Scarlet fever should not be confused with measles, as there is no true rash on the face. In some cases the erythema of scarlet fever may be blotchy enough on the limbs to suggest measles, although evenly spread on the trunk. The tongue may be similar in both diseases, but catarrhal signs and stomatitis will be lacking in scarlet fever.

Smallpox may be confused with measles at two stages of its development. There may be a morbilliform prodromal rash, but it is the papular stage of the true rash, particularly when it is profuse on the face, which causes the greatest difficulty. The eruption of smallpox is more shotty and it is not associated with catarrhal signs or fading Koplik's spots ; its distribution is different, for the rash shows a predilection for the extremities and tends to be scanty on the trunk. The subsequent development of papules into vesicles settles the issue.

The rose rash of the enteric group, which usually appears about the sixth day of disease, is sometimes profuse enough, particularly in paratyphoid fever, to suggest measles or rubella. The slow onset, the typical "staircase" rise of temperature, and the absence of catarrhal signs are against measles, and blood culture followed later by stool culture and Widal tests will confirm the diagnosis of enteric fever.

Another rash which is occasionally mistaken for measles is the haemorrhagic eruption of cerebrospinal fever, if it is at all profuse. This disease has a fulminating onset and there is usually early development of meningeal signs.

The rash produced by the sulphonamide group of drugs may bear a close resemblance to measles. Koplik's spots will be absent, however, and the eyes are usually clear. A history of taking the drug can usually be obtained, and such a history should always be sought in any doubtful case of measles. The barbiturates may give morbilliform rashes ; penicillin rashes are usually urticarial. Serum rashes resembling measles are seldom seen since the production of refined antitoxin, but sensitization to other foreign proteins may produce rashes of morbilliform type. These include areas of circinate or marginate erythema that are never seen in measles. Food rashes are either of this nature or urticarial.

Treatment

There is no specific treatment for measles, but patients with mild attacks recover quickly if kept warm in bed for a few days. Plenty of fresh air must be insisted upon. The diet in the early stages should consist mainly of milk with as much bland fluid, such as sweetened fruit drinks, as the child can be persuaded to take. A simple linctus may be necessary to control the cough if troublesome.

In the more severe cases, particularly if home conditions are not good, hospital treatment should be sought early. In such cases bacterial complications may be expected and a prophylactic course of a sulphonamide or, better still, penicillin should be given. For a child aged 2 years, for example, 0.5 g. of sulphadimidine thrice daily or 50,000 units of penicillin twice daily should be given for three or four days. The sulphonamide group should not be administered unless a sufficient fluid intake can be assured.

The Eyes.—There is usually severe photophobia, and the patient should be screened from strong light. The eyes should be bathed often and ung. hydrarg. ox. flav. smeared along the margin of the lids. Regular and careful inspection of the cornea is essential in order to detect the first sign of ulceration. This complication calls for specialist attention, but if this is not available the pupil should be dilated with atropine drops and hot bathings carried out two-hourly. "Albucid" or penicillin eye ointment should be instilled also.

The Mouth and Ears.—The hygiene of the mouth is particularly important, as there is always some degree of stomatitis and streptococci and other organisms abound there. In spite of these precautions otitis media may occur. It should be vigorously treated with penicillin systemically, and, if suppurative, by local drops into the ear. Failure of the discharge to clear up in a reasonable time is an

indication for operation, to remove the risk of a subsequent flare-up and to prevent the hearing being permanently affected. Deafness occurring in a young child will call for special education.

Laryngitis.—The early laryngitis of the prodromal stage usually needs no treatment, and signs of obstruction are slight or absent. The late laryngitis needs vigorous treatment. As soon as signs show themselves the patient should be given 20,000 units of diphtheria antitoxin intramuscularly. A course of penicillin should also be started —100,000 units six-hourly for the first twenty-four hours, and then twice daily. If there is much obstruction a steam tent may be helpful, and preparations for operative intervention should be put in hand. Tracheotomy is the operation of choice; the pneumonia which once followed so often can sometimes be avoided by vigorous chemotherapy. Intubation may induce ulceration of the larynx (if the condition is streptococcal ulceration may already be present) and lead to subsequent stenosis.

Bronchopneumonia. — Cases of bronchopneumonia should be nursed in the fresh air as much as possible, but guarded against chills. If more than slight cyanosis is present an oxygen tent is indicated. Full doses of sulphadimidine and penicillin should be given: for a child of two years, 0.5 g. of sulphadimidine and 50,000 units of penicillin six-hourly are advisable. The fluid intake must be adequate. If restlessness occurs small doses of potassium bromide or brandy may help. The latter is also of value if there is cardiac distress. Other useful adjuncts are tepid sponging, if the temperature is high, and kaolin poultices to the chest. If an empyema develops, frequent aspiration of the fluid, with penicillin replacement, may suffice without operative intervention being necessary.

Enteritis.—Infants who show signs of enteritis should immediately be given half-strength glucose-saline by mouth two-hourly; after this, third-strength "Benger's food" may be a useful stepping-stone back to normal feeds. If vomiting is a feature and dehydration develops, an intravenous drip transfusion of 5% glucose-saline, alternating with half-strength plasma, may be necessary.

Encephalitis.—There is no certain treatment for post-infective encephalitis. Convalescent serum from recovered cases of encephalitis has been tried, and thought by some to be of use. A lumbar puncture will be necessary for diagnostic purposes.

Convalescence.—A bad attack of measles will debilitate a child seriously, and a plentiful diet with adequate vitamins is necessary in the convalescent period. The child should be kept under observation, and if the lungs have been affected an *x*-ray examination should be made at the end of six months.

Terminal Disinfection.—Measles virus is short-lived and no special disinfection is necessary. Infected clothes and bedding should be washed, and the patient's room given a thorough cleaning.

Prevention

Isolation.—The prodromal stage of measles is so infectious that any child suspected of the disease should, if possible, be isolated from other children at once.

Passive Immunization.—If exposure to infection is known to have taken place a decision will have to be made whether protection by immune human serum should be undertaken. Such serum is very difficult to obtain at present, and for this reason the ordinary healthy child of 3 years or over will usually have to be allowed to take his chance. With infants and young children, especially those in a poor state of health or suffering from some other disease, every effort should be made to obtain enough serum for their protection. Whatever type is used it must be given in the first five days after exposure, the earlier the better: it is passive immunity which is being conferred, its duration is only about three weeks, and another exposure after this period may reinfect the child.

The following sera can be used:

	Protective dose up to 3 years	Protective dose after 3 years
Gamma globulin ..	2.5 ml. intramuscularly	Not determined
Convalescent serum	5 ml. „	(Age × 2) ml
Placental globulin ..	7.5 ml. „	(Age × 3) ml
Adult serum ..	10 ml. „	(Age × 4) ml

These sera, although scarce, can sometimes be obtained by application to a hospital or to one of the large commercial chemists.

Of the four types mentioned gamma globulin is probably the best. It is at least twice as strong as convalescent serum, and does not carry the risk of the other human sera —homologous serum jaundice. It must not be given intravenously.

Convalescent serum is obtained by bleeding a measles patient about the fourteenth day of disease, when the antibodies are at their highest level. It is at least half as strong again as placental globulin and twice as strong as serum from adults who have had measles in infancy (adult serum) No serum reaction may be expected from any of these, as they contain human, not horse, protein; but placental globulin may cause a rise in temperature.

If sera are not available whole blood from an adult with a known history of measles can be given intramuscularly, the dose required being double that of adult serum. The risk of giving Rh-positive blood to an Rh-negative female child must be guarded against. In any case the method is not satisfactory as it produces an artificial haematoma with its attendant dangers.

Attenuation.—If serum is available, attenuation rather than protection is a more satisfactory plan for children over 3 years. Half the full protective dose of serum should be given in the first five days after exposure. This is more economical than a full protective dose between the sixth and eighth day, though this will probably produce the same effect. The mild attack which results—if it is not too mild —will probably confer active immunity for life. With such a modified attack, however, though the child is not very ill, he is infectious and a risk to other children.

Notification.—Measles and whooping-cough were made notifiable in England and Wales in 1939. The information thus made available is of value to the public health authorities in the control of epidemics and in gathering epidemiological data.

In a booklet entitled *The Marriage Relationship* the Society of Friends emphasizes the importance of a religious background to life if marriage is to be successful. Surveying the causes of the breakdown of marriages, the report draws attention to inadequate preparation for marriage and lack of education in parenthood, housing, war and post-war conditions, and weakened belief in the permanent nature of marriage. Marriage guidance councils and other bodies are doing much helpful work, and "it should be increasingly realized that many of the difficulties encountered by young married couples could have been prevented by a talk with a suitably qualified doctor or some other experienced person before marriage." The booklet is obtainable for 9d. (postage 2d.) from the Friends Book Centre, Euston Road, London, N.W.1.

SOVIET BIOLOGY AND BRITISH COMMENTATORS

BY

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Russia Puts the Clock Back. By J. Langdon-Davies. (Pp. 160. 7s. 6d.) London: Victor Gollancz.

Soviet Genetics. By J. S. Huxley. (Pp. 245. 8s. 6d.) London: Chatto and Windus.

It has been uncharitably said of journalists that they feed, like vultures, on misfortune. In particular, the turbulent history of Soviet Russia has been a gold mine for scores of newspaper men. Each crisis in Moscow breeds a few books from western authors: the crisis in Soviet biology is no exception. Commentaries on Soviet biology are appearing already (half a dozen were published in English alone during 1949), and the reader may make a choice among sources of opinion ranging from genuine Communist to ultra-bourgeois.

The facts in the matter are these. All the reliable information about the recent crisis in Soviet biology has been before the British public for a year. The serious student of Russian affairs knows by now exactly where to find this information. Therefore the merit of any fresh writing on Soviet biology rests on one or other of two grounds: either fresh facts must be divulged or the familiar facts must be re-interpreted in the light of the writer's special knowledge of Russia or of biology. It is for these merits that the two books under review have to be examined.

Russia Puts the Clock Back offers a gloss on broadcasts about Lysenko by Harland, Darlington, Fisher, and Haldane, with a popular exposition of Mendelism. Mr. Langdon-Davies (unlike most geneticists) seems to regard Mendelism as sacrosanct, so that he feels obliged to defend it with the zeal of a mediaeval churchman defending orthodoxy. So far as the crisis in Soviet biology is concerned, Mr. Langdon-Davies is content to quote what British commentators have to say about second-hand reports of the crisis, and to comment himself upon the commentators.

Soviet Genetics is a serious study of the situation, and it can be recommended with confidence to readers who are not expert biologists. In the first place it summarizes very fairly the available published information, and it adds a few minor details from Dr. Huxley's own recent experience in the Soviet Union. In the second place it offers the reader an assessment of the facts by an expert, for Dr. Huxley has himself made major contributions to genetics. The book contains a lucid and objective account of the scientific issue and the ideological issue (wisely separated by Dr. Huxley) in the light of the available information. When he discusses biology Dr. Huxley is authoritative and scrupulously accurate, and when he discusses Russia he is much more modest and tentative than Mr. Langdon-Davies. The present persecution of Mendelian geneticists in Russia raises the controversy far above the level of a scientific dispute, and Dr. Huxley's indictment of the Soviet policy is amply justified.

Lysenko and Soviet Motives

When he lays down Dr. Huxley's book the reader feels he is familiar with the facts about the crisis in Soviet biology; but the motive behind it all is still elusive. No obvious interpretation arises from the facts as Dr. Huxley presents them. The Russians are intelligent and shrewd. Among them are scientists as gifted as any in the western world. And science enjoys a prestige in Russia far higher than in this country (for instance, some medical research workers receive from five to ten times the salary of general practitioners). Why, then, has the Russian Government attacked the very intellectual liberties which make scientific research possible? Why has it agreed to give public support to a fanatic whose scientific attainments would not qualify him for a junior post in a British university?

There is no unambiguous answer to these questions, but it is possible to suggest a tentative answer which is at any rate consistent with Russian behaviour in other matters. The first relevant fact is that Lysenko's diatribes against Mendelism are not original and they are not new. Thirty years ago articles indistinguishable from Lysenko's were appearing in the Tsarist press under the name of Michurin. Therefore hostility to Mendelism is not a monopoly of the Soviet Government: it lies deeper than that. Secondly, when one examines the content of both Michurin's and Lysenko's writing one finds (in the same flatulent style) the same appeal to practical results as the sole criterion of success in plant breeding, and the same indignation that theoreticians are interfering in affairs beyond their jurisdiction, and by doing so endangering the national food supply. Thirdly, there are still bread queues in Soviet Russia, and the efficiency of agricultural production is pitifully low. The Achilles heel of Soviet Russia is her food supply, and her food supply is in the hands of a very simple, ignorant, and lazy peasantry. When Lysenko comes among this peasantry with the zeal of a prophet, and with such maxims as "Keep down the weeds," "Space your millet more widely on dry soils," "Do not sow till soil temperatures are higher," he does accomplish what in Russia are miracles—he brings production up to something like the level of that in western countries.

Nowadays the whole atmosphere of agricultural extension work in Russia is as eager as that of a religious revival, and for this Lysenko is largely responsible. His importance to Russia at this stage cannot be overestimated. It is for this reason that one distinguished Soviet scientist, Zhukovsky, is reported to have said, in extenuation of the decision to suppress Mendelism, that it is important "at this juncture to cherish the prestige" of Lysenko. Of course it is: the alternative is longer bread queues.

Intellectual Climate in Russia

Among Western people the importance of a man like Lysenko to the national economy would not give weight to his views on topics outside his competence. But Russian people (as any student of Dostoievsky knows) are different. They plunge head and shoulders into hero-worship to a degree quite incomprehensible to the Englishman. We can admire Mr. Bernard Shaw and still say his opinions on evolution are piffling. We can load the honours of science on Sir Oliver Lodge and remain discreetly silent about his views on paranormal phenomena. But the intellectual climate in Russia is quite different. The mass of the people is so unsophisticated that the minute core of intelligentsia must still be careful to avoid puzzling inconsistencies. It would be disastrously puzzling to the Russian peasant if Lysenko were hailed as a great leader among collective farmers (which he is) and at the same time ridiculed as an impertinent upstart among geneticists (which he undoubtedly is). So "at this juncture" (and these are important words) the intelligentsia have to keep quiet about their views. Russia is not yet ready for her scientists.

There is no opportunity in a review such as this to cite the evidence for these assertions. But a good deal can be gathered from two books, both easily available to the British

reader. The first of these is *The Russian Peasant*, by Maynard—quite the best book ever written on Soviet agriculture (and it is no accident that Maynard took the Indian peasant, not the British farmer, as his standard of reference). The second is *A People's Academy*, by G. Fish, a blatant piece of Soviet propaganda, published in Russia for circulation among bourgeois countries. Presumably it tells us what the Russians would like us to know, but it is very easy to read between the lines how precarious the food situation is in Russia and what drastic steps have to be taken to increase production.

In this context the crisis in biology loses some of its gravity. Of course it is serious when one nation breaks away from one of the few remaining international liberties (for that is what science is). It is serious when a man can be persecuted for what he thinks. It is serious when dogma takes the place of fact. Most of us would deliberately prefer death to Soviet rule. But then we are not Russians.

TOXAEMIAS OF PREGNANCY

SYMPOSIUM AT CIBA FOUNDATION

A symposium on the toxaemias of pregnancy was held at the House of the Ciba Foundation on January 12, 13, and 14. Professors A. St. G. Huggett, W. C. W. Nixon, and E. C. Amoroso, in co-operation with Dr. G. E. W. Wolstenholme, secretary of the executive council of the Ciba Foundation, were responsible for organizing this symposium. In the invited audience there were physiologists, veterinarians, obstetricians, physicians, pathologists, endocrinologists, and biochemists.

Pathology of Pregnancy

At the first session, under the chairmanship of Dr. A. S. PARKES, F.R.S., Professor HUGGETT read a paper on the physiological changes in pregnancy. Like the chairman in his opening remarks, he paid tribute to the work of the late Professor W. H. Newton.

Professor H. L. SHEEHAN then described the pathological changes found in pre-eclampsia and eclampsia, excluding from consideration such related conditions as vomiting of late pregnancy, jaundice at delivery, hypertensive shock, accidental haemorrhage, massive liver necrosis, etc. He referred to the unsolved problem of oedema in these cases, and said that the remaining pathological lesions gave evidence of the vascular disturbances peculiar to hypertensive toxaemias in late pregnancy, and could be linked up with such signs and symptoms as albuminuria, oliguria, convulsions, and coma. In his view there was no real histological basis for the descriptions of "pregnancy kidney" found in the older literature. Chronic nephritis was a very rare pathological finding in cases of toxaemia. In eclampsia there were specific periportal lesions in the liver, but most focal lesions in fatal eclampsia occurred in the terminal stages. The extent of these lesions was not obviously related to the severity of the toxaemia or to the occurrence of fits.

Mr. G. W. THEOBALD in his paper stressed the changing incidence of pregnancy toxaemias in Siam and Hong Kong with alterations in the diet. Increased protein in the diet led to an increased incidence of toxaemia. There had also been an increase in the incidence of toxaemia with an increase in the cases of beriberi, but where beriberi was commonest the incidence of toxaemia was slight. In the same way there had been fewer cases of toxaemia in occupied Europe during the war, but there was a rapid return to pre-war figures with the return to a fuller diet.

Professor WILLIAM J. DIECKMANN discussed the aetiology of pre-eclampsia and eclampsia with particular reference to the sodium, potassium, and chloride balance. On January 11 he had lectured on this same theme at the Royal College of Obstetricians and Gynaecologists. He described how at the Chicago Lying-in Hospital they had devised a relatively safe method for the carefully controlled intravenous injection of sodium chloride solution. They had studied in cases of toxaemia changes in weight, oedema, alterations in blood pressure, proteinuria, and the onset of symptoms and signs associated with eclampsia, all of which were increased by inducing an abnormal balance of water and electrolytes.

Toxaemias in Animals

At the second session, with Dr. H. H. GREEN in the chair, Dr. H. B. PARRY described the toxaemias affecting sheep. He said there were two groups of disorders: First, in many species there was the group of conditions associated with mineral imbalance and causing neuromuscular disturbances, seen mainly at parturition and in the puerperium; included in this group were milk fever, lactation tetany, and lambing sickness. The second group of disorders was confined to ewes in the latter half of pregnancy and was manifested by stupor, blindness, ketosis, and—post mortem—a fatty liver. In large-scale field trials in Australia, with restriction of exercise in ewes with twins or a heavy single lamb, and with sudden changes of food intake, this second type of toxaemia had been induced experimentally.

Dr. A. T. PHILLIPSON said that in ewes a form of pregnancy toxaemia, with weakness, anorexia, deranged nervous co-ordination, ketonaemia and hypoglycaemia, acetone in the breath and ketonuria, and—post mortem—a grossly fatty liver, could be produced experimentally by certain feeding and fasting measures. This appeared to suggest that ewes in which the foetus made big demands developed toxaemia when they failed to accommodate sufficiently rapidly to sudden changes in diet.

Dr. J. DUCKWORTH emphasized the speed with which low calcium states could be induced. Very low calcium diets did not affect the health or reproductive capacity of rats, and had no effect upon the size or viability of the litter. But the withdrawal of minerals from the skeleton over three gestation-lactation cycles amounted to as much as 60%.

Dr. RUTH ALLCROFT described the neonatal ataxia of lambs. This was a type of spastic paralysis, due to hypocupraemia in the mothers, which were unaffected. A similar disorder in bovines also affected the calves only, but not as severely as the lambs. In affected lambs gross demyelination of whole hemispheres occurred.

Dr. A. MESSERVY discussed the practical problems of milk fever, which was due, in his opinion, to over-lactation. There was a satisfactory response to injections of glucose solution or to inflation of the udder, but it was also essential that the animals should be put out to grass.

Professor A. ROBERTSON, in a paper on the biochemical aspects of bovine parturient hypocalcaemia, mentioned some studies which were being made of blood calcium, phosphorus, and magnesium levels in normal bovine pregnancies and in cases of milk fever. Marked changes had been noted, but they were not regarded as primarily responsible for the condition, and an investigation of the hormonal factors that might be concerned had begun. He described some interesting changes in mineral balance after the treatment of milk fever by inflation of the udder.

Placental and Circulatory Changes

Professor F. J. BROWNE presided over the third session when Dr. N. FALKINER recounted how in human toxaemia the focus of interest had shifted from the kidney to the liver and later to the placenta. He believed all the changes in toxaemia were secondary to vascular disturbances consequent on arteriolar spasm. The placental changes could not be a matter of chance, and those who thought so were not familiar with the anatomy and the pathology of the placenta. He described in detail the anatomical features of the placenta, and the changes which he had found in cases of eclampsia. Acute yellow atropy and cortical necrosis he regarded as the acme of toxaemia and worthy of close investigation in connexion with eclampsia.

Professor R. J. KELLAR reported some studies of cardiac output and skin and muscle blood flow in normal and in toxaemic pregnancy. He gave some further details of the methods and findings of his co-workers, Dr. Hamilton and Dr. Burt. This Edinburgh work called forth high praise from Professor J. McMichael and Professor G. W. Pickering. Professor

DE WATTEVILLE (Geneva) mentioned his own studies of skin temperature by means of timed immersion in hot and cold water. There were significant differences in the times of return to normal temperature in cases of toxaemia.

Dr. C. SCHNEIDER (Detroit) described the factors normally concerned in coagulation and the changes which could be induced by injections of thromboplastin. Pathological changes in the placenta similar to those found in toxaemia had been produced in this way.

Professor VAN BOUWDIJK BASTIAANSE (Amsterdam), reading a paper on ischaemia of the gravid uterus as a probable factor in the causation of toxaemia, said that he believed that toxaemia of pregnancy was related to an absolute or relative insufficiency of the blood supply to the placenta. He described a series of experiments in pregnant dogs in which ischaemia of the uterus artificially induced by clamping branches of the uterine artery caused hypertension. He was now investigating the possibility of relieving toxaemia by increasing the blood supply to the uterus by, for example, the attachment of omentum.

Professor K. J. FRANKLIN said that Mr. Sophian had suggested to him a theory of the aetiology of eclampsia—namely, that distension of the uterus produced reflex constriction of the renal arteries and diversion of the renal cortical blood flow. Experimental distension of the uterus, bladder, or intestine caused visible blanching of the renal cortex.

Nutritional and Hormonal Studies

Dr. D. P. CUTHBERTSON presided at the fourth session, when Dr. L. E. GLYNN gave an account of work which he had undertaken in collaboration with Professor H. P. Himsworth. Extensive fatty infiltration of the liver had been produced by a deficiency of lipotrophic agents, and necrosis indistinguishable from acute yellow atrophy by a deficiency of protective sulphur-containing amino-acids. The combination of a thio-amino-acid and a vitamin E deficiency, an unusual state of affairs in pregnancy, since a marked vitamin E deficiency led to abortion, might account for the rare cases of acute yellow atrophy in pregnancy. Dietary factors might produce toxaemia indirectly by affecting the liver's power to metabolize hormones.

Dr. I. F. SOMMERVILLE laid much emphasis on unwarranted reliance on quantitative estimations of serum and urinary chorionic gonadotrophin, and of oestrogen and progesterone metabolites. Many workers had found low urinary values of pregnanediol in the toxaemias of pregnancy, theoretically due to renal retention (no evidence), low production (as thought by Smith and Smith), or abnormal metabolism (Marrian and Sommerville had some evidence of this in non-pregnant hypertension). He discussed the work of Smith and Smith, including that on the prevention of toxaemia by the intended stimulation of progesterone production by means of injections of stilboestrol.

Professor R. H. S. THOMPSON, discussing the mono-amine oxidase activity of the placenta, gave a detailed description of work at Guy's Hospital on estimations of mono-amine oxidases in the uterus. Since hypertension was a factor in toxaemia, it was important to find out whether the placenta, like the kidney, contained enzymes capable of oxidizing and inactivating amine pressor substances. Enzyme deficiencies, or excessive production of the pressor substances, would cause hypertension. Oxygen tensions would clearly also play a part in inactivation by such enzymes, which had been found particularly in the endometrium of the uterus in rats and rabbits.

Dr. LARS WERKO (Stockholm) described work done with Dr. Axel Ahlmark on histaminase in normal and pathological pregnancy. There was evidence that the histaminolytic activity of serum might be greatly altered in cases of toxaemia, but the changes were irregular and not related to the severity of the toxaemia.

Final Session

Sir HENRY DALE presided over the closing session. Dr. JOHN HAMMOND presented a diagrammatic summary of the possible underlying mechanism by which varying dietary changes and deficiencies might produce toxaemias in animals, through the competition of various tissues and the foetus for nutrients. There followed a lively discussion in which Dr. Hammond's theorizing was regarded as too simplified, a view with which Dr. Hammond himself agreed.

Professor G. W. PICKERING then protested against the use of the term "toxaemia" as indicating a spurious unity of diverse conditions and also suggesting a causative factor. He distinguished between acute yellow atrophy, Wernicke's encephalopathy, and pre-eclamptic eclampsia, and confined his remarks to the latter condition. Fits might occur in acute nephritis and in malignant hypertension, and it was assumed that they were due to oedema of the brain. According to Sheehan, there was no evidence of oedema of the brain, and, according to Kellar, the blood flow in the brain was not markedly diminished during fits. The cardiac output increased in pre-eclampsia and there was no other condition known where hypertension and increased cardiac output were combined. He had never seen spasm of the retinal arteries in pregnancy toxaemia. Circulatory disturbances in pre-eclampsia as judged by clearance tests were not the same as those in essential hypertension. This was probably due to some factor in the placenta, since it is also found in cases of hydatidiform mole. There were hormonal and enzyme changes in the placenta, but there was no evidence that they were primarily responsible for toxaemia. There was no evidence, at least in the early stages, of any cortico-medullary shunt.

Professor F. J. BROWNE congratulated all the previous speakers on their researches, but he emphasized the defects in existing knowledge and in some instances the need for confirmation of results. He refused to give up the use of the word "toxaemia," and wanted to know what factor other than a toxin affected the capillaries of the glomeruli. How could Professor Bastiaanse's theory explain toxaemia arising three days after parturition? How did Dr. Schneider's thromboplastin injections produce high blood pressure or oedema? What was the real incidence of placental infarcts in toxaemia in Dr. Falkiner's cases? Professor Dieckmann's saline injections caused hypertension, but clinical hypertension was found before any oedema could be noted by inspection, or by recording changes in weight. Mr. Theobald had mentioned that toxaemia was fifteen times more common in connexion with beriberi, but it could not be prevented by the administration of vitamin B_1 or the B complex.

There was again a lively discussion which was brought to an end by the chairman. Sir HENRY DALE said that all enjoyed this agreeable and informative meeting of experts. He welcomed particularly the opportunity the symposium had provided for joint consultation between students of animal and human biology. Generous acknowledgments were due to Professor Huggett, the chief organizer, and to the secretary and staff of the Ciba Foundation.

In connexion with this symposium a reception was held by the Trustees of the Foundation, represented by Lord Beveridge and Lord Horder, to which all who took part in the three-day meeting were invited as well as a number of other distinguished guests.

Reports of Societies

BIOCHEMICAL TREATMENT OF ALCOHOLISM

A lecture by Dr. ERIK JACOBSEN, of Copenhagen, on biochemical methods in the treatment of alcoholism was given on January 10 at a joint meeting of the Section of Psychiatry (Royal Society of Medicine) and the Society for the Study of Addiction. Dr. W. J. T. KIMBER presided. The lecture had special reference to "antabuse," the proprietary name for tetraethylthiuramdisulphide, the use of which in the treatment of alcoholism was described by Dr. A. E. Carver in a recent paper in the *Journal* (August 27, 1949, p. 466).

Dr. Jacobsen said that although his address was on the subject of biochemical methods he fully acknowledged that such methods must be accompanied and followed by psychotherapy, about which he knew little. He outlined the internal and external factors concerned in alcoholism. Probably there was no single cause, and both sets of factors operated in different proportions according to the individual's make-up and environment.

Alconolism led to neuroses, which themselves reinforced the internal factors (anxiety states, and so on) which had helped to bring about the first resort to alcohol, and it also made worse the external factors (social and family conditions) which again had had their share in causation. Some general physicians believed that it was sufficient to deprive the patient of alcohol, but experience showed that deprivation alone would produce only temporary relief.

He went on to describe the pharmacological action of the sulphide compound. Tablets of "antabuse" were innocuous, or produced no more than slight digestive trouble, when taken alone, but if alcohol was taken afterwards, even no more than an ounce (30 ml.) of whisky, the pulse rose sharply, and the patient noted palpitations and increased discomfort, with a constricted feeling in the neck, and frequently nausea and vomiting. The effect of 40 ml. of gin taken after the administration of 1 g. of "antabuse" was graphically illustrated. The compound interfered with the normal metabolism of alcohol, causing unusually high levels of acetaldehyde to be present in the blood.

Results of Treatment

The results with 200 alcoholic patients, taken as they came, without special selection, and treated in Dr. Martensen-Larsen's clinic in Denmark, were described. The treatment was modified until a maintenance dose of "antabuse" was reached, and this was continued for some months according to the requirements of the patient. Meantime psychotherapeutic and social measures were undertaken. The nature of his addiction was explained to the patient, who was told that his constitution was such that he must avoid alcohol. Group therapy had proved useful. A guardian was appointed for each patient—wife, friend, or employer—to watch over the treatment and report to the doctor if anything went wrong.

Of these first 200 patients, 17 were seen only for a short time, so that a proper regime could not be instituted; another 16 disappeared from view; three died, one of them committing suicide. There remained 164, of whom 112 had been observed for twelve months and 52 for nine months. Only about 10% of the patients were women. In the group studied 92 patients had a family history of alcoholism; 107 had neurotic symptoms; 89 had started drinking to compensate for disabilities; in 136 there was no abuse of other drugs; 125 had a low critical dosage for alcohol; 72 were mainly home drinkers and 92 outdoor drinkers; 43 drank habitually, and 26 only at the week-end; 90 patients had been the subject of earlier inconclusive attempts at treatment.

Of the 112 who had been observed for 12 months, 52.2% made a full social recovery; 17.3% showed a large measure of improvement; 11.6% some improvement; and the remainder were unchanged. Young patients had a much better prognosis than the elderly; recovery was effected in 76% of the patients under 36, and in only 44% of those over 51. Where some other treatment had been tried previously results were just as good as in those patients treated for the first time. Of those who took the tablets regularly, 67% had recovered within nine months; of those who ceased to take the tablets before the end of the desired period only 29% recovered.

Dr. Jacobsen agreed that "antabuse" in itself was not a cure for addiction; it must be used in conjunction with other methods. If it was given without warning the patient, it might provoke acute reactions and make it more difficult to give proper treatment later. "Antabuse" should not be given except with the patient's full consent. The aim must be to re-educate the patient and help him to live an alcohol-free life. New interests must replace the interest in alcohol. "Antabuse" could break the vicious circle and assist in the re-establishment of family and social position. The third and fourth months of treatment were the most critical for many patients.

In most cases any original psychological difficulties seemed to fade when the addiction was brought to an end. It was, of course, impossible to continue with "antabuse" indefinitely, but to reach a stage at which the patient could be declared recovered and taken off "antabuse" was itself of great therapeutic value. About half the 200 patients had continued the treatment for from seven to nine months, but there was much individual variation, and some had continued under treatment for the full twelve months. Dr. Jacobsen admitted that the number of observed patients was still too small and the time too short to make more than tentative conclusions justifiable. Therapy must be individual, and the results depended to a very large extent on the team work of doctors and social workers and on facilities for group therapy.

Dr. H. PULLAR-STRECKER, honorary secretary of the Society for the Study of Addiction, described "antabuse" as the first antidote to alcoholism which had been effectively used in treatment—a point of view which was contested by a later speaker, who mentioned apomorphine. Dr. Pullar-Strecker also said that tetraethylthiuramdisulphide had been used for years in the vulcanization of rubber, and it was well known to factory doctors that men working with this substance often developed a repugnance to alcohol. He thought that for some patients—namely, those who would do anything to throw off their handicap but could not help themselves—it might be described not as an adjuvant but as a therapy in its own right.

In a brief discussion Dr. A. E. CARVER pointed out the value of the drug in indicating lapses in patients under treatment. Some speakers mentioned possible ill effects. Dr. ROBERT ORTON, while he thought the method a useful ancillary, mentioned a few cases in which disturbing toxic symptoms had appeared. One patient developed marked diplopia, and another, after a trial dose of alcohol after "antabuse," developed a left facial palsy.

VETERINARY OBSTETRICS

The president, Mr. S. B. HERD, took the chair at a meeting of the North of England Obstetrical and Gynaecological Society held in the Liverpool Medical Institute on December 16, 1949.

The president chose as the subject for his address "Veterinary Obstetrics." Sterility, he said, which was not uncommon in animals, was tackled vigorously by the veterinary surgeons and was of considerable commercial importance. Hydramnios and oedema were sometimes noted during pregnancy, but did not seem to be associated with toxaemia, nor was there any record of associated foetal deformities. The animal had no apprehension regarding labour, and labour was relatively short, especially in the mare; the pelvic floor did not present problems due to rigidity and animals were quite often delivered standing. Whether the cord snapped or was divided by the teeth, haemorrhage did not occur. The freemartin, the female twin when one twin was of either sex, was always sterile as a result of the mixed circulation and presented interesting characteristics. Finally, Mr. Herd paid tribute to the efficiency of those engaged in veterinary practice and said that although it was probably not necessary for obstetricians to have the same physical strength they and the obstetricians had much in common.

The presidential address was preceded by an account of a case of intraperitoneal bleeding during pregnancy from a ruptured uterine vein, by Mr. J. GARDINER WIGLEY and Mr. R. W. BURSLEM. A case of spontaneous annular detachment of the cervix was also described by Miss U. M. LISTER.

For the last ten years the Ministry of Food has published a weekly bulletin for the interest of the Ministry's staff. It is now available to the general public (H.M.S.O., 4d.). The first public number (January 7, No. 528) includes an interesting account of how the Ministry controls meat and livestock. The article opens with the words—more forbidding perhaps to the bulletin's new public than to readers in the Ministry—"The meat and livestock control scheme is one of the closest controls exercised by the Ministry," and it goes on to describe how the Ministry "acquires physical possession of all beef, mutton, veal, and pork, whether home-produced or imported, and also all canned corned meat." Purchase and transport are described, and also the fate of such by-products as skins, which go to tanners and fell-mongers, pig and sheep gut, which is used for sausage casings, and glands, which are used for medical purposes.

Correspondence

Fifty Years of Ophthalmology

SIR,—Your annotation on "Fifty Years of Ophthalmology" (January 7, p. 69) is not quite accurate about the popularization of the intracapsular extraction of cataract. In all fairness I think that the credit for the popularization of this operation should be given to the late Lieutenant-Colonel Henry Smith, of the Indian Medical Service. In 1903 he published a report of 6,500 intracapsular operations done by him in India (*British Medical Journal*, 1903, **2**, 719). Although many ophthalmologists did not approve of his technique, yet they set out to obtain the same results by safer procedures for the extraction of cataract by the intracapsular method.

The intracapsular extraction of cataract was carried out in India many years before it became popular in Europe. Lieutenant-Colonel N. C. MacNamara, the first whole-time professor of ophthalmology at the Medical College, Calcutta, practised it freely during the period of his professorship from 1867 to 1874. He practised the removal of the cataractous lens by extraction with a horn scoop without iridectomy for all forms of cataract, and advocated the removal of the lens in its capsule in cases of immature cataract causing considerable impairment of vision, so that none of the soft and transparent cortical matter might attach itself to the iris.

Lieutenant-Colonel Molroney, working in the Punjab, India, also practised the intracapsular extraction of cataract freely before Smith's time. He did not, however, publish any work on the subject.—I am, etc.,

London, W.1. E. W. O'G. KIRWAN.

The Short Oesophagus

SIR,—Drs. J. B. Rennie, Frank T. Land, and S. D. Scott Park (December 24, 1949, p. 1443) have usefully stressed the importance of considering the short-oesophagus syndrome when investigating a patient with upper-alimentary-tract symptoms. There are, however, many statements in their article with which I have to disagree, and I deplore the impression given of the absence of any specific treatment.

First, on a point of terminology I would submit that the term "gastric hernia through the oesophageal hiatus," implying as it does a primary defect in the diaphragm, is a misnomer when discussing the short-oesophagus syndrome. Whereas herniation may truly be said to exist in the oesophago-gastric variety of thoracic gastric loculus, it is, I believe, due to the very fact that the oesophageal hiatus is normally constituted and the diaphragmatic muscle not weakened that symptoms develop in patients with a short oesophagus.

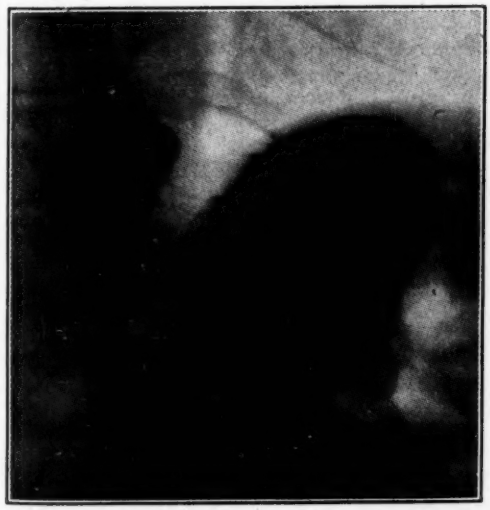

FIG. 1.—Female aged 48 with symptoms dating from childhood. Radiograph taken in horizontal position.

The point of constriction is usually not at the oesophago-gastric junction, as indicated in Fig. 1*c* of the article, but at the level where the stomach passes through the diaphragm. This point is clearly illustrated in the accompanying radiograph (Fig. 1).

Secondly, I would not agree from my experience that dysphagia was the commonest presenting feature in the short-oesophagus syndrome. Of eighteen cases I have studied nine have been entirely symptomless—the abnormality only being discovered on searching for a source of chronic blood loss in a patient presenting with iron deficiency anaemia. Of the remainder, dysphagia was only complained of spontaneously in three instances, and the usual story was of indigestion dating from childhood but differing from ulcer distress in an absence of complete remissions, in the position of the pain, in the lack of response to the taking of alkalis or food, and in the absence of true night pain. The relief of pain that followed vomiting was usually dramatic and often enabled a patient to complete a meal previously abandoned because of pain and rapid satiation of appetite. The similarity between the quality of the pain experienced by these patients and that occurring in peptic ulceration has always appeared to me as strong support for the view that ulcer pain is related more to changes in intragastric tension than levels of acidity.

Finally, I would suggest that no patient with a short oesophagus should be discharged from hospital without determining the effect of left-sided phrenic-nerve interruption. This form of treatment is not new, but apparently many physicians and surgeons are unaware of its value. It has been condemned as unphysiological by those who use the term diaphragmatic herniation, but this criticism loses all validity if it be appreciated that the primary defect in these patients is the congenitally short oesophagus. Whatever the theory, the proof of the treatment is in the results obtained. Not always does re-examination demonstrate such a satisfactory result as is seen in Fig. 2, but even when a considerable portion of the stomach remains above the paralysed diaphragm relief of symptoms is usually complete. This relief of symptoms may be regarded as due to a decrease in the constricting effect of the oesophageal hiatus on the stomach.—I am, etc.,

FIG. 2.—Same patient as in Fig. 1. Radiograph taken one week after left phrenic crush. The stomach remained entirely below the diaphragm even on firm abdominal pressure with the patient in a head-down position.

Edgware, Middlesex. G. M. BARRETT.

SIR,—In the leading article on "The Short Oesophagus and Hiatus Hernia" (December 31, 1949, p. 1517) your statement, "The diagnosis of hiatus hernia requires special radiological technique, and it is the responsibility of the clinician to remind the radiologist of its likelihood, for routine barium meals in a busy department may fail to demonstrate the herniation," cannot be allowed to pass without comment. Hiatus hernia is not difficult to demonstrate provided the gastric examination is complete, with the patient supine and prone as well as erect and the films taken under fluoroscopic control.

Pressure of work on a busy department should not be allowed to cut down the quality of the examinations. An incomplete

examination can be a most dangerous and misleading procedure, and pressure to "simplify" the examination to deal with increased numbers must be resisted. There can be no short cut to a radiological diagnosis. A patient may have two lesions: to find one only is not enough.—I am, etc.,

Barnet, Herts. CEDRIC HILLIARD.

Failed Forceps

SIR,—While I agree with much of Mr. Bryan Williams's letter (December 10, 1949, p. 1353), I cannot agree that manual rotation of deep transverse arrest of the head is "usually impossible, and that attempts to carry it out are dangerous." In my experience a true persistent occipito-posterior is relatively rare, and deep transverse arrest, or oblique arrest, is infinitely commoner.

The difficulty and danger of manual rotation depends upon many factors, but, assuming a reasonable size and shape at the plane of least dimensions and at the outlet, certain predisposing factors may occur. First, early rupture of the membranes followed by a long and tedious labour. Secondly, allowing the head to remain visible at the vulva for a long time without any advance, and particularly when the patient has been encouraged to push without first ascertaining whether the sagittal suture is antero-posterior, oblique, or transverse. Thirdly, fatness of the vaginal subcutaneous tissues, combined with caput formation. Any obstetrician of experience will recognize this syndrome—the dry tense vagina, the tense moulded foetal skull with a large caput, and the uterus which is clamped down on the baby's body.

It is not always possible to eliminate this state of affairs, particularly in the patient who has very early rupture of the membranes and tense soft parts. It is, however, possible to avoid the long continuance of a deep transverse arrest which has occurred as a mere accident at the end of an otherwise normal labour. It has always seemed to me that the average midwife is far too prone to tell the patient to push down without first ascertaining the exact position of the sagittal suture. To tell her to do so with a transverse arrest is useless, misguided, and lethal.

I have only failed to rotate a deep transverse arrest on three occasions during the last seven years; and on only one occasion, in which, incidentally, I was able to perform rotation quite easily, have I had a stillbirth. This occurred as a result of cord prolapse during the rotation. In two of my three failures this outcome was anticipated, by virtue of the pelvic type with *x*-ray pelvimetry, and these were both treated easily, and successfully for both mother and baby, by lower-segment caesarean section. The third was delivered with some difficulty with Kielland's forceps, the baby surviving a most stormy labour. This patient had a simple flat pelvis, and I had never set eyes on her till I was called upon to effect delivery late in the second stage of labour. I subsequently delivered her twice more by elective lower-segment caesarean section.

I agree with Mr. Williams that Kielland's forceps effect delivery easily in most cases, but not many have had the good fortune to be shown exactly how to use this instrument at first hand as I was by my friend Mr. Barton Gilbert many years ago. In the hands of a trainee Kielland's forceps can undoubtedly do harm, and for such a one manual rotation is in my opinion safer for both mother and baby, and not at all the lethal and difficult operation that he would have us believe. Finally, that great master, Smellie, gives us good advice on this very subject, and it is well worth while quoting his directions in full.[1]

"In the year 1749 I was called to a woman who had been long in labour of her first child. . . I attended some time without perceiving that the head advanced to open the os externum [perineum]. I felt one of the ears at the os pubis, and lambdoidal crossing the end of the sagittal suture, at the lower part of the right os ischium, and the fontanel on the opposite side at the upper part of the left. I perceived that the pains had not force enough to move the occiput from the right ischium, so as to pass under the os pubis, and the forehead from the opposite side to the hollow of the sacrum; I therefore, during the next pain, introduced my fingers towards the child's left temple, and turned the forehead backwards to the os sacrum. The narrow part of the head being now towards the sides and lower part of the pelvis, the vertex immediately advanced forwards, gradually opening the os externum during every pain; and the woman being safely delivered, the placenta separated slowly, and was discharged in about half an hour."

So much for this "newly described" condition now called deep transverse arrest. I would like finally to draw attention to a most useful method of delivery by the ordinary obstetric forceps, which is carefully described by Caldwell, Moloy, and Diesopo[2] in an article entitled "Pelvic Arrests." This consists simply in drawing down the head gently in the transverse position, and is quite easy of performance if the subpubic arch is wide, as it is, for instance, in flat pelves. The occiput is then found to rotate by itself under the lower part of the arch, or may easily be turned by hand at that level.—I am, etc.,

London, W.1. D. G. WILSON CLYNE.

REFERENCES

1 *Treatise on the Theory and Practice of Midwifery*, New Sydenham Society. London, 1877, **2**, 183.
2 *Amer. J. Obstet. Gynec.*, 1938, **36**, 928.

Development of Psychological Medicine

SIR,—Dr. John Rickman, in his contribution "The Development of Psychological Medicine" (January 7, p. 30), which is of course essentially a masterly essay on the development of psycho-analysis, writes: "In the thirty-five years in which Jung's views have been developed . . . they have never attained such strength of articulation as to embody a quarterly journal or any cohesive library series of books; the absence of such collective and conscious utterance puts the views of this school at a disadvantage."

Dr. Rickman is to be congratulated on the fairness of the second sentence. The essence of the first is, factually, correct and leads to the view that Jung is "complicated," "mystical," and esoteric, which is untrue, as everyone can find out for himself by reading books like Jung's *Modern Man in Search of a Soul* and *Essays on Contemporary Events*, Esther Harding's *The Way of all Women*, Gerhard Adler's *Studies in Analytical Psychology*, or Michael Fordham's *The Life of Childhood*, to name a few. The reasons for the absence of a journal or a series of publications are manifold, one being the probably greater introversion of the Jungian. The greater extraversion of the Freudian has the opposite results. Incidentally, there is an annual in the German language, the *Eranos Jahrbuch*, which has regularly appeared since 1933. Unfortunately it is not translated, though it contains French and English contributions.—I am, etc.,

Dumfries. D. J. SALFIELD.

SIR,—At the beginning of the second paragraph of his paper on this subject (January 7, p. 30) Dr. John Rickman writes, "This article does not touch on the development of psychiatry"—and indeed it does not. There is no mention of the development of physical methods of treatment, even the least controversial of them, such as the malaria treatment of G.P.I. or the use of our growing knowledge of endocrinology, nutrition, or electrophysiology.

There is a passing reference to Kretschmer, but nothing is said of the advances in the study of constitution and genetics that have been made since his pioneer work. The change of atmosphere in mental hospitals is attributed to the diffusion of Freud's ideas, but it had begun before he was heard of and has been greatly influenced by many workers who have, rightly or wrongly, shown little interest in Freud's theories or have maintained the attitude of benevolent scepticism which was all he asked of his patients and critics. Nothing is said about the development of child guidance, the changed approach to juvenile delinquency, or the changes in public opinion as shown by the growth of the mental hygiene movement in the U.S.A. and the National Association for Mental Health and the Mental After-Care Association in this country. The growth of epileptic colonies, the provision of educational facilities for backward children, the development of psychiatry in the armed Forces and of industrial psychology in civil life, are also passed by.

"Psychosomatic" medicine (which surely deserves to be called psychological medicine if anything does) is left out. Could there not have been also some reference to the improved quality of mental nurses and to the growth of that young profession which has in such a short time so deservedly won the confidence and gratitude of psychiatrists and the public—the psychiatric social workers?

Dr. Rickman has, in fact, written of the development of psycho-analysis, and nobody is better qualified to do so. But it is a pity that your "Fifty Years of Medicine" number did not include a review of the development of psychiatry. This would include an impressive body of material which would interest (and perhaps convince) the general reader more than an account of the development of one school of psychopathological theory.—I am, etc.,

London, S.W.3. D. S. MACPHAIL.

*** The signed articles in the symposium on "Fifty Years of Medicine" were concerned with the outstanding developments of the past fifty years. Of these, the work of Freud was merely one. Many of the points made by Dr. Macphail were dealt with in the leading article "Progress in Psychiatry."—ED., *B.M.J.*

The Fate of the Foreskin

SIR,—I should like to range my popgun alongside Dr. Douglas Gairdner's cannonade (December 24, 1949, p. 1434) and join in his volley against the respectable bastions of infantile circumcision. Dr. Gairdner refers to 54 boys between 2 months and 3 years referred for circumcision, in all but one of whom the prepuce could readily be retracted after separation with a blunt probe. Records are not immediately available to me, but I can state that during two years as a senior hospital resident I was requested to perform circumcision on infants (children over 1 year being admitted and not all seen by me) at the rate of two or three each week. No infant under the age of 3 months could be seen, on account of the waiting-list. My practice was to carry out gentle separation of the prepuce, as described by Dr. Gairdner, in order to retract it and apply antiseptic to the glans and preputial skin preparatory to operation. In not one of the series of two hundred or so did I find difficulty in retracting the foreskin. This awoke in me the suspicion—since strengthened by fifteen months' specialized experience of paediatrics—that infantile circumcision is an unwarranted surgical procedure.

On the other hand, a comfortably remote acquaintance with troops serving in North Africa suggested to me that ritual circumcision among nomadic tribes in the Middle East, with inferior bathing facilities, was as sound a precaution in the second world war as in the forty years' wandering.—I am, etc.,

Birmingham. BRIAN WEBBER.

SIR,—We think that Dr. Douglas Gairdner's interesting article on the prepuce (December 24, 1949, p. 1433) neglects one or two points. It is easy in the infant (if one has spent some time in "Casualty" selecting candidates for circumcision) to distinguish two types. In the first, on attempting to retract the prepuce, its margin thins, a little of the glans becomes visible, and one can feel that a little more proximal traction would peel the prepuce back—i.e., it is simply adherent or, as Dr. Gairdner points out, not separated.

In the second, on attempting to retract, the margin of the prepuce does not thin so much, a definite constriction is usually visible just proximal to the margin, which is a little bulbous beyond it, and, in any case, one can feel that further traction meets with a definite resistance, preventing the preputial orifice from enlarging. This is true phimosis. We do not think a probe is necessary to make this distinction.

That the first type should be treated conservatively, it is easy to agree. The point is whether the second type later becomes retractable. Through not distinguishing these types in his Table (Fig. 5) Dr. Gairdner throws no light on this point. If these are the persistent 10%, then, as they are easy to recognize, it would appear simplest to circumcise them in infancy.

It is true that after circumcision one occasionally finds the glans very raw and slow to heal (say two or three weeks), which would be accounted for by Dr. Gairdner's histological facts. But we find this uncommon, perhaps in about one case in six, and not occurring necessarily in the younger victims. Might it not sometimes be the result of leaving the prepuce adherent for too long?

Furthermore, our impression is that older children (of two or three years) are more likely to get post-operative sepsis and delayed healing and also (this is more than an impression) are much more difficult for the mother to manage during the two or three weeks required for healing. For these reasons it is the practice in the hospital in which we work to circumcise infants with true phimosis.—We are, etc.,

H. M. ROSE.
London, S.E.13. A. M. GOULD.

SIR,—Dr. D. Gairdner's paper (December 24, 1949, p. 1433) has dealt comprehensively with an operation which has become little more than a vogue. It is indeed appropriate that some attention should be drawn to the fact that circumcision is needlessly performed in the vast majority of cases.

The main pretext upon which this operation is performed is undoubtedly the so-called "non-retractable" foreskin. I would add to Dr. Gairdner's figure of 10% of non-retractable foreskins in boys of 3 years of age by saying that at least 25% of foreskins at this age have not yet become completely separated from the glans penis. The older view that the presence of the foreskin initiates and encourages masturbation is still present amongst anxious and ignorant parents; yet their own forcible manipulations of the infant's prepuce are more likely to encourage this habit, even if it was harmful.

I would also add to Dr. Gairdner's sequelae of circumcision by pointing out that in 80–85% of developed meatal ulcers meatal strictures also develop. It is for these strictures that meatotomy is so frequently performed, the vast majority of these patients having been circumcised in infancy. Congenital meatal stricture is a rarity. I remember some years ago presiding over an out-patient clinic to which a young mother brought her 3-year-old son and requested circumcision of the boy. Finding no reason whatever why the perfectly mobile and clean prepuce should be removed, I asked why she wanted the operation performed. She replied, "Oh, it looks so much nicer."

This attitude towards sexual cosmetics is more primitive. It is generally the circumcised fathers who desire a similar mutilation of their sons. If 84% of public-school boys are circumcised it is time that doctors enlightened them on the anatomical functions of the prepuce and the importance of hygiene rather than subject their male offspring to this fashionable mutilation.—I am, etc.,

Newcastle-upon-Tyne. J. W. PERROTT.

Insufficient Anaesthesia

SIR,—At the present time anaesthesia for prolonged abdominal cases commonly consists of heavy curarization with minimal narcosis. Like many other anaesthetists I am an enthusiastic advocate of this technique, but as the following case will show one must be reasonably certain that the level of narcosis does not become too light.

The patient, an intelligent and co-operative woman aged 46, underwent laparotomy for suspected carcinoma of the head of the pancreas. Premedication was morphine 1/6 gr. (11 mg.), atropine 1/100 gr. (0.65 mg.), and she was slightly more drowsy than the average when she arrived in the anaesthetic room. Induction was with "tubarine" 15 mg. (after 5-mg. test dose) and 0.4 g. of thiopentone. A No. 9 cuffed tube was easily inserted and directly connected to a Coxeter-Mushin absorber. Nitrous oxide and oxygen 500 ml. of each per minute were run into the circuit and respiration was aided throughout the operation. Small doses of thiopentone and tubarine were given into the drip as required, to the total of 0.8 g. and 65 mg. respectively. Subtotal pancreatectomy was carried out by Professor Charles Wells. During the first three hours the gas mixture was unaltered, but during the fourth hour oxygen alone was given. During the last half-hour (before and during wound closure) 20% cyclopropane was administered. Prostigmin 5 mg. and atropine 1/50 gr. (1.3 mg.) were given during skin suture. The patient's post-operative course was good.

I saw the patient on the third day after operation and during conversation casually inquired about when she came round. Her reply was somewhat shattering—"As a matter of fact, doctor, I woke up in the theatre! I remember going to sleep after your injection in my arm, and some time later I was awakened by the most excruciating pain in my tummy. It felt as if my whole inside were

being pulled out: I wanted to cry out or otherwise indicate my suffering, but I couldn't move any part of me. I heard the doctors talking about the gall-bladder and about doing something with it to the small intestine. Then I went to sleep again and later on woke up back here in bed." She said she had never before experienced such short-lived agony, and it was obvious that the pain must have been severe, because she appeared to have very little post-operative pain or discomfort—i.e., she was a woman with a high pain threshold. It is reasonably clear from the foregoing that her period of consciousness coincided with the absence of nitrous oxide from the mixture, and that the cyclopropane was adequate to induce further sleep for the conclusion of the operation. At no time during operation was her respiratory excursion less than about 20% of normal, and during the fourth hour she twitched her eyebrows twice: on each occasion 1 ml. of 5% thiopentone was given. By itself it was obviously insufficient; if the nitrous oxide had been maintained she would still have twitched her eyebrows (as patients often do with this anaesthetic technique) but she would not actually have wakened nor would she have had any recollection afterwards. As she had diabetes the use of even a slight trace of ether was precluded, and long-continued cyclopropane, even in a low percentage, was not considered owing to the possible nuisance of increased oozing.

If faced with a similar type of case again, I should perhaps be a little more generous with the thiopentone, but the main requirement is to maintain the nitrous oxide unless the patient is obviously and grossly anaemic. I should be most interested to learn if any other anaesthetists have had the similar misfortune of having a curarized patient very definitely conscious at some stage of an operative procedure.—I am, etc.,

Liverpool. E. H. WINTERBOTTOM.

Second Thoughts on Streptomycin

SIR,—Having just returned from Canada and the U.S.A., where I studied the chemotherapy of tuberculosis, I was extremely interested to see a note under "Medical News" headed "Second Thoughts on Streptomycin" in the *Journal* of December 3, 1949 (p. 1303). Perhaps readers would be interested to hear that the Eighth Streptomycin Conference held on November 10–13, 1949, in Atlanta, Georgia, was a most important meeting, at which the whole field of chemotherapy of tuberculous diseases was discussed, and the views of this conference are now being extensively quoted in the U.S.A. Your quotation, ". . . Results now reported appear to indicate that it (dihydrostreptomycin) has no important advantage over streptomycin, and that . . . its use in preference to streptomycin should not be encouraged," seems to be the general consensus of opinion regarding these substances in both Canada and America, as it seems to be in this country also. It would appear to be more than worth while to record, however, that at the Mayo Clinic the views of the chest physicians are in direct contrast to the statement quoted, and it is dihydrostreptomycin which is by far the most widely used. The workers at the Mayo Clinic maintain that it produces so much less toxic effects that its use would seem to be indicated and encouraged. —I am, etc.,

London, S.E.12. M. M. NAGLEY.

Streptomycin in Tuberculous Meningitis

SIR,—All writers seem agreed that intrathecal streptomycin is absolutely essential in the early stages of the treatment of tuberculous meningitis. The injection of a substance into the spinal canal is attended by a certain risk at any time and leaves a doubt in the mind if death should occur within a short time of administration. It is my experience with intrathecal streptomycin that deaths—when they occur—take place at an earlier stage than was the rule in untreated cases. These difficulties would be largely overcome if intrathecal injections could be avoided. The following case is not put forward as a reason for abandoning intrathecal streptomycin—not by any means. It is given as an example of the necessity for early diagnosis in this condition and for the early removal to hospital of suspected cases, for in certain cases, in the initial stages, it may yet be found safe to rely on intramuscular injections alone.

A schoolgirl aged 9 years was admitted to hospital on September 23, 1949, suffering from queried meningitis. She was then three days ill, complaining of headache, lassitude, and loss of appetite. A sister had died some years previously from meningitis, probably tuberculous. On examination she was well nourished, but was somewhat confused. There was ptosis of the left eyelid; neck rigidity was present and Kernig's sign was positive. Temperature was 100.4° F. (38° C.), and the pulse rate was 90. Lumbar puncture revealed a clear fluid under pressure. Pending the bacteriologist's report this was regarded as a case of tuberculous meningitis. Treatment was commenced with intramuscular injections of dihydrostreptomycin—1 g. in 24 hours in divided doses at 8-hourly intervals. Gradually the patient became more acutely ill. On the third day in hospital she was vomiting continually and temperature was 103° F. (39.4° C.) She was now very confused. The bacteriologist's report on the C.S.F. was: fluid clear, cells 10, chlorides 700, globulin slight trace, sugar normal, acid-fast bacilli present. There was no change in her condition until the sixth day of treatment, when her temperature fell to 99.4° F. (37.4° C.). As a result of this improvement the decision to give intrathecal streptomycin was deferred until the following day, when, her condition being much better, it was abandoned. On this day temperature was normal, vomiting ceased, and she was less confused. Thereafter she rapidly regained normal health, and there has been no set-back up to the time of writing. Eight-hourly injections were continued for six weeks, for the remaining eight weeks 0.5 g. was given every 12 hours intramuscularly. The report on the C.S.F. on October 19 was: cells 2, globulin trace, sugar normal. chlorides 740, no gross pleocytosis, no tubercle or other organisms. A similar report has been more recently received. The patient was allowed out of bed on December 16. She was able to walk quite well in a few days, and had put on weight. Clinical examination revealed nothing abnormal in central nervous or other systems. Report on *x*-ray examination of lungs: enlarged left hilar shadow—both lung fields clear. There was no local or general reaction to injections at any time.

This case is considered remarkable, as there appears to be a complete recovery from a condition proved clinically and bacteriologically to be tuberculous meningitis, and especially as treatment was confined to intramuscular injections. There can be no doubt that intrathecal therapy is essential in established cases. Is there a possibility that it can be avoided in the very early stages?—I am, etc.,

Swinford Co. Mayo, Ireland. PHILIP F. CAWLEY.

Anticoagulant Therapy

SIR,—There are one or two points in the paper on anticoagulant therapy by Drs. H. W. Fullerton and G. Anastasopoulos (December 31, 1949, p. 1492) which concern my original article in the *Journal of Clinical Pathology* (1949, **2**, 45) and to which I should like to draw your attention. They state that haemolysis shortens the accelerated clotting time with the venom method, probably because of lipoid set free from the cell envelope. They state that added lipoid (as in alimentary lipaemia) produces little or no shortening of the accelerated clotting time when the effects of dicoumarol are marked. They then say that the results obtained by me with the venom test in patients on dicoumarol should be discounted because I "was obviously producing varying degrees of haemolysis." As the differences which I reported between the venom and the brain-extract tests were in patients fully under the influence of dicoumarol and not in normal individuals there seems, Sir, to be some inconsistency here.

As to the haemolysis which Drs. Fullerton and Anastasopoulos suppose to have been present, Wintrobe's anticoagulant (which I employed) is widely used in blood work and does not cause haemolysis. Further, the word "shaken," used in my original paper, does not necessarily imply violent agitation, and the blood was actually mixed by inversion. Lastly, the results obtained by me—namely, less lengthening of the accelerated clotting time with the venom test than with the brain-extract test, and sluggish response of the venom test to the effects of dicoumarol—are actually confirmed by Drs. Fullerton and Anastasopoulos in this paper, as will be seen by reference to their conclusions and to Chart III respectively. Consequently it is with pleasure (having in mind the safety of patients on dicoumarol) that I note from this paper that Dr. Fullerton does not now use the venom test alone in the control of dicoumarol therapy.—I am, etc.,

London, W.9. G. A. JAMES.

Pruritus Vulvae

SIR,—Professor T. N. A. Jeffcoate (November 26, 1949, p. 1196) has drawn attention to two causes of pruritus vulvae which are apt to be overlooked. The first is trichomonas infection of the vagina, and the second is intermittent glycosuria, which can easily be overlooked in a routine examination of the urine. His remarks on leukoplakia, however, appear to perpetuate the loose thinking and therefore confusing terminology that surround this subject. If the word leukoplakia is to mean anything it should be applied to changes comparable to those found on the lips, mouth, and tongue, and known to be precancerous. When uncomplicated by maceration or secondary infection leukoplakia, both in the mouth and vulva, has a characteristic clinical and microscopical appearance. The affected area is bluish-white. The microscopical appearances are also diagnostic, but because these are insufficiently recognized and inadequately studied in the vulva much of the present confusion persists. Even when complicated by gross intertrigo, however, the microscopical appearances are characteristic if an adequate examination is made. This may, however, require more than one biopsy.

In leukoplakia the epidermis is hyperplastic to variable degree and is characterized by its irregular lower border with pointed, often branching, downward prolongations, lack of definition of its basal layer, and often slight atypicality of its cells. The horny layer is well formed and thickened, often grossly so. Hyperplastic areas are frequently set in the midst of atrophic epidermis, which is apparently their precursor. The superficial dermis underlying leukoplakic epidermis shows hyalinization of collagen, reduction or complete loss of elastic tissue, and a non-specific infiltration by chronic inflammatory cells. Since leukoplakia has such a sinister prognosis, thorough investigation seems indicated. It should, moreover, serve to draw attention to the existence of leukoplakia as a distinct entity by differentiation from similar white appearances of the vulva with which it is now so often confused.

Professor Jeffcoate himself seems guilty of some ambiguity when he states that: "There is good reason to believe that it may not be a specific entity but merely one type of skin reaction to many possible stimuli: prolonged scratching alone can produce somewhat similar skin changes. It is sometimes the result of vitamin-A deficiency, and is also seen occasionally in various types of anaemia and in diabetes." The evidence brought forward hitherto to support these suggestions is slight. Again he records that: "One of the most typical cases of 'leukoplakia' I have ever seen was in a doctor's wife who suffered from vitamin-B deficiency as a result of a diet which consisted almost entirely of a few water-biscuits a day. The administration of riboflavin quickly restored the vulval skin to normal." This must be an unusual experience, and it would be interesting to know whether this diagnosis was confirmed by microscopy. He makes no mention of the normal waxing and waning, both of signs and symptoms, in leukoplakia.

While agreeing with Professor Jeffcoate that leukoplakia may occur at any age, there does seem to be some reason for supposing that occasionally endocrine defect does play some part. The maximal incidence of leukoplakia is undoubtedly about or after the menopause, and it is not infrequently found in association with a premature menopause. I agree with Professor Jeffcoate, however, that endocrine treatment does not seem to be of any value in this disorder.

In his discussion on the causes of pruritus vulvae, Professor Jeffcoate makes no mention of the atrophic form of scleroderma, known as lichen sclerosus, which frequently affects the anogenital region and often gives rise to intense pruritus. With regard to the administration of hydrochloric acid by mouth for obscure and intractable pruritus vulvae, and without commenting on the somewhat flimsy theoretical premise on which this treatment is based (and to which Professor Jeffcoate himself draws attention), he is, I think, more fortunate in his results in a gynaecological clinic than in a comparable series seen in a dermatological out-patient department. Moreover, he makes no mention of the psychological effect of a pleasant doctor fortified by an exceedingly unpleasant medicine. Having justly condemned indiscriminate *x*-ray treatment, Professor Jeffcoate fails to mention it for the form of vulval skin disorder in which it is most helpful, namely neurodermatitis. Both clinically and histologically this may closely simulate intertrigo and leukoplakia.

Much of the difficulty in the aetiology of pruritus vulvae, if not the therapeutics, would be greatly helped by adequate combined study in gynaecological and dermatological clinics.—I am, etc.,

London, W.1. H. J. WALLACE.

New Mechanism of Vitamin Deprivation

SIR,—Dr. P. Ellinger in his second letter (December 31, 1949, p. 1529) persists in his misinterpretation of my paper (October 1, 1949, p. 731). It now appears, however, that Dr. Ellinger did not intend to comment on the main substance of my paper at all, but only on the title, the introduction, and the last paragraph of the discussion.

By any ordinary interpretation of the English language the title of my paper implies that its substance is concerned with vitamin deprivation in the sprue syndrome. In fact, all the evidence put forward and 80% of the discussion was in reference to the sprue syndrome alone. The introductory paragraphs give a brief general survey of the accepted mechanisms of vitamin deprivation. This section was intended for those readers of your *Journal* who may not possess specialized knowledge of vitamin problems. General consideration of these mechanisms is clearly relevant to, and a proper introduction for, a paper in which the mechanism of vitamin deprivation in the sprue syndrome is discussed. Dr. Ellinger is wrong when he says that deficiencies of vitamins A and D are "entirely unconnected with the sprue syndrome." The last paragraph of the discussion in my paper refers to a number of conditions which Sir Philip Manson-Bahr and other authorities consider to be closely related to the sprue syndrome. I expressed the hope that some of those who are better placed than I am to study these conditions would give some consideration to the possibility of the mechanism of vitamin deprivation proposed in my paper. Differences between these various conditions and the sprue syndrome are, of course, very relevant to the sprue problem itself.

Dr. Ellinger clearly does not understand the points contained in my previous letter (December 3, 1949, p. 1294) which refer to possible differences between dietary vitamins and vitamin precursors and synthetic materials and to the difficulties of interpreting effects due to administration by different routes. We seem to disagree on the use of the term "normal" as applied to human subjects. A subject is not strictly normal if his diet is deficient in certain vitamins or if he is consuming succinyl-sulphathiazole. The various papers referred to were presumably written to point out the way in which these experimental subjects differed from normal. That they were physically fit is quite beside the point. Dr. Ellinger now states that he never intended his comments to refer to the sprue syndrome, which was the subject of my paper. In the same paragraph in his letter, however, he dismisses my reply, in which I pointed out that his comments were not applicable to the sprue syndrome, as "invalid." Of course, if Dr. Ellinger's remarks have nothing to do with the sprue syndrome there is not much that can be usefully discussed in either of his two letters.

Dr. Ellinger's real worry seems to be about what he likes to call my "claim to have made a new discovery." I do not "withdraw or deny" anything. Such a claim would be entirely contrary to the attitude I have always adopted with regard to scientific research. For the twenty years I have been engaged in scientific research I have always been glad to discuss the work I am doing with any scientific colleagues who are interested and to give any help I can to those who are genuinely concerned with solving problems of mutual interest. I have always been, and I shall continue to be, opposed to all restrictive practices in scientific research, among which I include individual claims to original ideas or "discoveries" and the assumption of proprietary rights in any particular field of work by any person or group. The suggestion that I put forward any claim to a new discovery in my paper on vitamin deprivation is a pure

invention on the part of Dr. Ellinger, and one which I entirely repudiate.

Freedom of scientific discussion is the very root from which the tree of scientific knowledge grows—on that tree ideas blossom and some bear fruit. Can anyone reasonably claim to being entirely responsible for one particular flower on this tree? Should one not feel satisfied if one can make some slight contribution to the growth and well-being of the tree as a whole which may help in some measure to bring many flowers to fruition? Complete freedom of scientific discussion is an ideal which may be difficult to attain in a prestige-ridden world, torn by conflicting economies and ideologies. The field of medical science is one, however, in which we can do something to strive towards this ideal upon which the future progress of science so largely depends.—I am, etc.,

Birmingham. A. C. FRAZER.

*** This correspondence is now closed.—ED., *B.M.J.*

Hormones and Rheumatism

SIR,—Dr. William Hughes's letter (December 31, 1949, p. 1527) is a valuable comment on the work of Professor Selye and certainly suggests that factors other than the release of adrenocortical hormone play a part in the prevention and, likewise, in the temporary suppression of rheumatic manifestations. We must surely all agree that rheumatism of joints, whether chronic or acute, is a local tissue reaction. This therefore must depend on the ability of the tissues involved to react. Logically, then, the depression caused by a severe intercurrent disease might be expected to relieve the symptoms of an arthritis. All rheumatologists must have come across arthritics who, when down with influenza, thought their arthritis was cured, since all the pain and much of the disability had temporarily disappeared. In view of Professor Selye's work there are now two possible explanations: release of hormone under stress, and debility causing a general lowering of local tissue reaction.

Some experiments which I carried out in 1928[1] on rabbits can, to my mind, only be explained on the assumption of lowered tissue reaction. At the time injections of various strains of non-haemolytic streptococci were being given to a large series of animals in order to determine which of these had a predilection for bone tissue. A number of strains were found to be "osteo-tropic," and in fact regularly produced arthritis when injected intravenously. Professor H. A. Harris suggested to me that if the rabbits were first fed on a non-vitamin dietary lesions might appear more rapidly. This was done. After a few weeks the rabbits, having lost weight, began to look ill: the fur was rough and staring. These were then injected parallel with a series of normally fed rabbits, and the net result was that the normal rabbits all developed arthritis in the usual way, whereas the "deficiency" rabbits hardly developed any arthritis at all. A somewhat similar observation made at the Pirbright Experimental Station[2] was to the effect that cattle and other large animals do not react well to inoculation with the virus of foot-and-mouth disease when they are in low condition; and in all outbreaks high-class stock, fed and kept in the best conditions, suffer more severely than lean beasts when the disease is allowed to run its course.—I am, etc.,

London, W.1. H. WARREN CROWE.

REFERENCES

1. *Ann. Pickett-Thomson Research Lab.*, 1929, **4**, 398 and 445.
2. *Proc. R. Soc. Med.*, 1937, **30**, 1049.

The Acute Throat

SIR,—The armed Forces provide perhaps the only opportunity in this country of treating large numbers of cases of tonsillitis in hospital. As M.O. in charge of a tonsillitis ward for nearly a year I have followed the correspondence in your columns with great interest. Neither in the original article nor the subsequent correspondence on tonsillitis has any suggestion been made of a method of treatment which I have found efficacious in the majority of patients—viz., 600,000 units of penicillin in aqueous solution immediately, followed by 200,000 units twice daily to a total of 1,600,000–2,000,000 units, supported by gargles and symptomatic treatment. The penicillin is given by intramuscular injection.

I have adopted this as a routine for the following reasons: (1) it is as effective as sulphonamides or penicillin (in whatever dosage) administered more frequently; (2) it involves minimal disturbance of the patient; (3) minimal co-operation by the patient is required; (4) the high initial dose almost invariably brings about dramatic relief of toxaemia and subjective improvement; (5) bacteriology is comparatively unimportant, as Vincent's organisms respond as rapidly as streptococci.

There is but one of the many aspects of the problem I would further like to comment upon. In his letter (November 19, 1949, p. 1179) Dr. Thomas Anderson implies that his advice to 70% of his patients would be: "Go home, gargle, and strengthen your defences." It is surely only when his sore throat has failed to subside after 24–48 hours (and usually longer), but has in fact got worse, that the patient consults his doctor. Rigors and severe dysphagia call for more active treatment, even though only "the usual throat commensals" can be demonstrated, as is more frequently the case than not.—I am, etc.,

London, S.E.18. E. L. W. L. LOMBAY, Captain, R.A.M.C.

Antihistamine Drugs and the Common Cold

SIR,—As the original sponsor of the use of antihistaminics in the treatment of the so-called common cold (April 17, 1948, p. 758), I should like to answer Dr. H. M. Stanley Turner (January 14, p. 129) on the confusion he states has arisen. I can reassure him that no confusion exists as regards the aetiology of histamine activity in this condition, nor in the proper manner of administration of antihistaminics in its successful treatment.

In my opinion the only confusion is due to both professional and public laxity in the use of the term "cold," this term being applied to almost any condition, with or without rhinorrhoea, ranging from an acute laryngitis to exacerbation of a chronic frontal sinusitis. One might equally as foolishly term any febrile condition as a "hot." The term vasomotor rhinitis is almost equally as vague. Surely this is merely an acute response of the body defences to some irritant of the nasal mucosa to which the particular individual is sensitive or allergic.

The local biological changes of histamine activity, followed by vasodilatation and rhinorrhoea, are identically the same when produced by an allergen as also occur in the initial phases of the so-called common cold produced by either virus or other irritant. This is the precise reason why an antihistaminic and vasoconstrictor applied locally in the early stages will abort the condition and so prevent the secondary stage of air-borne infection with subsequent mucopurulent catarrh.

Would it not remove a great deal of confusion if we abandoned these vague terms and retained the old term acute rhinorrhoea—it being only a symptom, as is jaundice—and classify its aetiology according to its causative agents, either allergic or non-allergic? I feel that only in this way shall we view the use of antihistaminics in the abortion of acute rhinorrhoea in its true perspective.—I am, etc.,

Whitburn, Co. Durham. F. CORT.

*** A question about the treatment of colds with antihistamine drugs is answered this week in "Any Questions?" (p. 261).—ED. *B.M.J.*

Analgesia in Childbirth

SIR,—To favour chloroform in labour, administered by an anaesthetist or by a general practitioner, may class one among the diehards, but it is still possible to remain faithful to the analgesic recommended to us as students by a nephew of Sir James Simpson. Attendance at 1,792 childbirths, where chloroform was almost invariably given, without any effect upon the child and with, as a result, the death of only one mother (from acute yellow atrophy of the liver), together with a total administration of chloroform on 3,319 separate occasions in hospital and general practice, all tends to give confidence.

I feel that I cannot altogether subscribe to the dictum of Dr. C. Langton Hewer (December 31, 1949, p. 1521) that "chloroform is a toxic drug to both mother and child and its use is not to be encouraged."—I am, etc.,

Aberdour, Fife. J. B. PRIMMER.

Vitamin C and Benzene Poisoning

SIR,—The annotation on vitamin C and benzene poisoning (December 31, 1949, p. 1520) reminds me that during the last war those of us working in filling factories found some evidence that ascorbic acid was useful in the prevention and treatment of poisoning due to trinitrotoluene. This was first suggested by my colleague, Dr. J. H. Watson, in 1941, and in the following year Dr. (now Professor) R. E. Lane, of Manchester, at a meeting of the Royal Society of Medicine, stated that the treatment of toxic jaundice included "a high carbohydrate diet low in fat with high vitamin B and C intake."

Aplastic anaemia, the symptoms of which resemble scurvy, is produced by the prolonged exposure to benzene. It is also caused by absorption of T.N.T., which is a nitro-derivative of benzene. While benzene itself as a solvent has been largely abandoned in industry on account of its dangers, its homologues and derivatives are still widely used and toxic effects sometimes occur. Ascorbic acid may act by assisting the excretion of these poisons from the body, but further work is undoubtedly needed to determine its exact role in detoxication.—I am, etc.,

Edinburgh. CATHERINE SWANSTON.

Rh Genotype Tests

SIR,—I was interested in the case described by Dr. T. H. Boon (December 17, 1949, p. 1417). The case which I described was heard during March, 1949, so that my statement that it was the first case of this kind heard in a British court is probably correct. The question of priority is, however, not important. I published this case so that others might have a precedent to which to refer when they were preparing evidence on Rh blood groups in connexion with disputed paternity.

It is important that this evidence should come to be accepted as at least the equivalent of the testimony of eye witnesses. This will occur only as a result of the accumulation and recording of cases. From this point of view Dr. Boon's case is important. I am not quite sure from Dr. Boon's letter exactly what was at issue in his case, but it appears to have been a civil action. If so I think it is the first time that evidence on Rh subgroups has been accepted in a British civil court. I am very glad, therefore, that Dr. Boon has recorded this case and I hope that all subsequent cases will be described either in the medical or in the legal journals.—I am, etc.,

Glasgow, W.2. EDGAR RENTOUL.

An Offending Article

SIR,—I feel I must draw attention to what I believe to be a potent source of serious infection in the majority of homes. The offending article is the brush which is used for cleaning the w.c. basin. It is the practice to keep this utensil in an open container adjacent to the water-closet, where it is freely available to flies and other vectors of disease.

Moreover, it is the habit in many households to hang the brush out of the bathroom window; in fact many music-hall jokes have been made about the practice. The position, however, as I see it, is far from a joke. In the majority of houses the w.c. is situated immediately above the scullery or kitchen, so that, especially in hot weather, it is but a short trip for flies to pass from the highly infected bristles of the brush to the food being prepared or stored below.

It seems to me irrational to focus attention upon the hygiene of the toilet, such as the washing of hands after use of the w.c., if a more serious and potent source of disease is to be neglected. In my opinion, much of the acute gastro-enteritis, enteric infections, and even infantile paralysis is highly likely to be spread in this way.

The situation could be met by one of the following: (1) to use no brush at all, the brush to be replaced by a powerful chemical cleanser, (2) to use a brush which is kept submerged in a strong antiseptic within an airtight container; (3) to develop a high-powered water jet which could be attached by a rubber tube to the wash-basin tap in those cases where there is a tap adjacent to the w.c.—I am, etc.,

Newport, I.O.W. JOHN MILLS.

The Medical Artists' Association of Great Britain

SIR,—I would like to draw the attention of the medical profession to the existence of this association, which was founded at Oxford on April 2, 1949. Until the present time those people who have become medical artists have mostly drifted into this profession more or less by accident. Many of them have had no contact with the other members of their profession, and some have only undertaken medical work on a part-time basis. While a few have not only received a thorough grounding in fine art but also have served an apprenticeship in medical work under an expert teacher, there are others, and among them must be included some really competent artists, who are entirely self-taught.

In view of these facts it is not surprising that there is a great variation in the quality of work which has been produced, but I think it is correct to say that the best medical work produced in this country can stand comparison with that produced anywhere in the world. Although there are quite a few medical artists who are very skilful in one particular branch of their subject—either in anatomical, in surgical, in clinical, or in pathological work—there are relatively few who have had that comprehensive training which makes them first-rate all-rounders. It is only in those hospitals and institutions which have the good fortune to employ a first-rate all-rounder that the usefulness of medical art in aiding the medical staff in their work is fully appreciated, but I believe that if more of such artists were available they would be able to make a valuable contribution to the work of the medical profession.

The future of medical art must depend largely on active co-operation from the medical profession and hospital committees. Only intelligent and artistically gifted people are capable of being trained as medical artists. They must start young, and their initial training must consist of at least three years' study of general art, followed by two years' training in medical work, under the constant supervision of a first-class medical artist. At this moment some of the best medical artists are training a few carefully selected pupils in medical art. If a number of hospitals and institutions were prepared to inform this association that they would be willing to engage a full-time medical artist, provided that a satisfactory candidate were available, and to keep this offer open, if necessary for a period of years, then the Medical Artists' Association on its side will guarantee to produce suitable candidates to fill the posts in the course of the next few years. But this association is not prepared to recommend second-rate people for any such posts as may become available, and so there would inevitably be a time lag while the association sought out suitably gifted artists and arranged the necessary course of instruction in medical art for them.

If the future of medical art is to be on sure foundations some regular provision must be made for the training of future artists, and we suggest that one centre of medical illustration should be recognized as the British School of Medical Art, and that all pupils should receive their training at this centre. Even if the demand for medical artists in this country did not justify such a school accepting more than about six pupils at any one time it would nevertheless serve a very useful purpose. A special advantage of such a school would be that it could keep closely in touch with the demand for medical artists through liaison with all centres where they are employed, and so limit its intake of pupils accordingly.

The executive committee of the Medical Artists' Association considers that the University of Edinburgh is the most suitable place for such a school of medical art, for Mr. Shepley, who is not only medical artist to the University of Edinburgh but also vice-chairman of this association, already has four pupils. The three-year course which he runs in medical illustration is recognized by the University of Edinburgh as a certificated course for fee-paying students. And in addition to this Sir James

Learmonth, professor of surgery at Edinburgh, has honoured this association by consenting to become its honorary president. It is only right that I should say here that the Medical Artists' Association is already indebted to Sir James Learmonth not only for valuable advice and moral support but also for very real and material assistance.

Our assistant secretary, Miss Audrey Arnott, who is medical artist to Oxford University and works at the Radcliffe Infirmary, is willing to supply members of the medical profession with the names and addresses of those medical artists who are members of this association, together with details of the type of work at which they are proficient. For many years to come there is bound to exist a considerable variation in the quality of work produced, but it is the policy of this association from the beginning to admit to membership only artists who really understand the special requirements of medical work. It is hoped that this information service will represent the first of many concrete services which the Medical Artists' Association will be able to render to the medical profession. An exhibition of medical art by members of the M.A.A. will be held at the Royal Society of Medicine from March 27 to April 1.

In conclusion I should like to say that I shall be happy to meet at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, any doctors or artists who would like to know more about this association.—I am, etc.,

D. H. TOMPSETT,
Chairman of Medical Artists' Association of Great Britain.

London, W.C.2.

Family Welfare Centres in Manchester

SIR,—Some of your readers interested in social medicine may have listened to the B.B.C. broadcast, "Focus on Marriage Guidance," on December 28, 1949. This ably presented account of some of the problems encountered made reference to the fact that the work of the National Marriage Guidance Council, the Roman Catholic Marriage Guidance, and the Family Welfare Association is Government sponsored.

I should like to call the attention of your readers to the fact that the Manchester City Council, on the advice of Dr. Metcalfe Brown, has for the last two years given increasing financial aid to the still partly voluntary work of the Family Welfare Centres in Manchester, now entering on their third year. They should not be confused with the Family Welfare Association, with which they are in no way connected.

The idea of these centres, which are housed in child-welfare buildings, originated from my knowledge and early experience of maternity and child-welfare work many years ago. The scope of our work is on broad lines, and its aim is to promote the unity and stability of family life. Help and advice are available free to anyone with a family problem from school-leaving age upwards. All the applicants are interviewed by doctors with psychiatric training.

My object in writing this letter is to make known the existence of this work and the encouraging support given to it by the Manchester City Council. It would seem unfair if their generous and far-sighted independent action should remain without acknowledgment.—I am, etc.,

GERTRUDE JEFFERSON.

Manchester.

Students' Literary Style

SIR,—We should like to know whether the student of to-day writes a worse paper than the student of twenty-five years ago, and, if so, why? In reading our students' scripts we have too often been struck by the poverty of style and vocabulary, by faults in spelling, and by general failure to present a considered and lucid answer to the question asked.

It would be interesting to know how far these deficiencies are general and to what extent they are of recent origin. If any of your readers still have unselected scripts submitted by students twenty and thirty years ago we should welcome the opportunity of reading them. If it then appeared that a significant deterioration has taken place it might be profitable to try to trace its causes.—We are, etc.,

CHARLES WELLS.
JOHN A. SHEPHERD.

Liverpool.

POINTS FROM LETTERS

The Uses of Streptomycin

Dr. KENNETH I. E. MACLEOD (Brighton, Mich., U.S.A.) writes: It may be of only academic interest to me, but nevertheless I felt so irritated by the latest presumptions and conceits of the medical hierarchy who, working within the various committees of the National Health Service, now rule medical practice in Great Britain, I just had to have my say. Now with the full powers and blessings of the legal word these self-important, autocratic men and women arbitrarily assume, incidentally casting still further aspersions on British medical education, that the average British general practitioner is not only ill-trained but is also little better than an ignorant, irresponsible fool, and certainly not a person to be allowed to meddle with such a dangerous drug as, for example, streptomycin. The list is growing and will continue to grow. No longer allowed to attend his patients in the many hospitals throughout the land wherein formerly he attended them, the modern British practitioner—this overworked, spineless sorting-clerk—may shortly find that he is too infantile to be entrusted with such dangerous procedures as intravenous therapy and so forth. . . . Only when given the fullest clinical responsibility can British general practitioners be expected to give of their best. We all can make our mistakes, the body specialist not the least. Perhaps they are making their greatest mistake now in condoning, if not actually encouraging, these backward trends.

Spoons as a Measure

Dr. A. J. K. DREW (Ramsgate) writes: Dr. E. H. Jeanes (December 17, 1949, p. 1418) mentions as a myth that the tablespoon contains half an ounce of fluid and states that it actually contains one ounce. The fact is that there are three sizes of tablespoons, and also of dessert and teaspoons. In a manufacturer's catalogue of cutlery I once saw the spoons listed, each in three sizes, the smallest of each being official and holding one, two, and four fluid drachms respectively. The medium size held 1½, 3, and 6 fluid drachms, while the largest size held double the smallest—viz., two, four, and eight fluid drachms. Most spoons I have seen in patients' houses seem to be the middle size, though I presume those belonging to Dr. Jeanes are the large variety. When I find patients finishing a bottle of medicine suspiciously quickly I always ask them to check the spoon they use and frequently find that they are not using the official size.

Use and Abuse of Vitamins

Dr. H. R. B. GIBSON writes from Monte Carlo: Professor L. S. P. Davidson (November 5, 1949, p. 1036) makes no reference to the influence of age on vitamin absorption. My work is chiefly amongst the elderly, the old, and the very old, and the benefit which so often results from the administration of Vitamins B and C to old people seems more than a coincidence. . . . My latest case is a lady of 98 years of age who developed some muscular weakness and increasing difficulty in swallowing. She had a healthy appetite. Vitamin B (100 mg.) and vitamin C (400 mg.) daily were given, and at the end of a week the dysphagia had gone and the mentality changed from despair to brightness. Other cases are less dramatic but point to the value of administering vitamins B and C in vague cases of unfitness in the elderly and old.

The Ageing Population

Dr. J. FINLAY ALEXANDER (Sevenoaks, Kent) writes: On looking through some old death-certificate books, I found one of 1945 in which the ages seemed to be unusually high. The book was of the small type for twenty entries, and on working out the average age I found it to be 78¼ years. The lowest age was 23, and the next 68. This seems to be a very high figure for twenty consecutive entries. . . .

Tablets in Cellophane

Dr. T. STRATON (Fordingbridge, Hants) writes: I find the growing tendency of tablet manufacturers to imprison their tablets in individual wrappings extremely irritating. There may be a theoretical hygienic reason for this type of wrapping, but I feel sure there can be little or no practical advantage. From a physical point of view these wrappings are usually quite infuriating to undo. . . .

Fifty Years of Ophthalmology

Dr. W. G. HUTTON (Newton Abbot, Devon) writes: I was surprised to find no mention in your leading article (January 7, p. 69) of advances made in the treatment of heterophoria and strabismus by means of orthoptic exercises. This omission seems characteristic of the general lack of interest in school and child-welfare ophthalmic matters so frequently shown in official circles.

Obituary

W. S. LAZARUS-BARLOW, M.D., F.R.C.P.

Dr. W. S. Lazarus-Barlow, who was until 1924 professor of experimental pathology in London University and an outstanding worker in the field of cancer research, died in a nursing-home at Bexhill on January 15 at the age of 84.

Walter Sydney Lazarus-Barlow was born on July 18, 1865, the third son of John and Martha Lazarus. On his twenty-first birthday he assumed by deed poll his mother's maiden name of Barlow and became the first to bear the surname Lazarus-Barlow. His father was a Christian Jew whose ancestry was believed to go back direct to Moses Maimonides; on his conversion he came to England from Russia and acquired British nationality. His early education was undertaken by his mother, from whom he received a sound grounding in history, French, and German. He then entered the City of London School, where in 1884 he won a minor scholarship, and later a foundation scholarship, at Downing College, Cambridge. Lazarus-Barlow did his clinical work as a student at St. George's Hospital. He graduated M.B., B.Ch. in 1889, proceeding M.D. in 1894. He was a house-physician at the Brompton Hospital, and later was appointed assistant curator of the Museum at St. George's Hospital under Humphry Davy Rolleston, as he then was. Towards the end of 1892 he was offered an unpaid research post by C. S. Roy, the professor of pathology at Cambridge, and thus started his work in this branch of medicine. Later in 1893 he was appointed demonstrator in pathology at a salary of £100 per annum and an examiner in public health at £60 per annum. Professor Roy died soon after this, and it was the rule then that when a new professor was elected all subordinate offices became vacant. Lazarus-Barlow was not re-elected, and for eighteen months he applied for post after post without success. Finally he was appointed curator of St. George's Museum at an annual salary of £50 and pathologist and lecturer in pathology at the Westminster Hospital at a salary of £250 per annum.

Lazarus-Barlow was elected F.R.C.P. in 1901, and in that same year he pricked his thumb at a post-mortem examination, as a result of which he lost his left arm above the elbow. After convalescing he returned to the Westminster Hospital until 1903, when he was appointed director of the newly created Cancer Research Laboratories at the Middlesex Hospital. Here he worked until he retired, and many Middlesex men, later to become well known in the medical world, worked under him in the ever-growing laboratories. In 1909 Lazarus-Barlow delivered the Croonian Lectures before the Royal College of Physicians, taking as his subject "Radioactivity and Carcinoma." After the 1914–18 war, during which he served for two years as a captain in the R.A.M.C. in France, he was appointed professor of experimental pathology at the Middlesex Hospital and held this post until his retirement in June, 1924. Lazarus-Barlow published a large number of papers, the early ones covering a wide range of subjects and the later ones almost all on some aspect of cancer research. In 1898 he published *A Manual of General Pathology*, which went into a second edition, and in 1903 *The Elements of Pathological Anatomy and Histology for Students*. He was president of the Section of Pathology and Bacteriology at the Annual Meeting of the B.M.A. in 1914, and president of the Section of Pathology of the Royal Society of Medicine in 1920. From 1923 to 1925 he was on the Council of the Royal College of Physicians. He was also a member of the Grand Council of the British Empire Cancer Campaign and a member of the Cancer Committee of the Ministry of Health.

In his private life Lazarus-Barlow devoted himself to his family, his home, and, in later life, his grandchildren. On his retirement he lived in a small cottage in Essex with two acres of garden, and here he edited the section on medical sciences of the fourteenth edition of the *Encyclopaedia Britannica*. His life was full and happy until July, 1946, when his only daughter died. He never fully recovered from this blow, which, together with some retinal haemorrhages and a series of minor cerebral lesions, made life a burden. He carried on as best he could for the sake of his wife until, five weeks before his death, he took to his bed. His brain remained clear to the last, and he constantly amused his nurses with his classical allusions and remarks on medicine in general. He leaves a widow and one son.

HERBERT E. BATTEN, F.R.C.S.

Mr. Herbert E. Batten, who died at his home in London on January 8, was consulting orthopaedic surgeon to the Charing Cross Hospital. He retired from the active staff in 1937.

Herbert Ernest Batten was born in Ilminster, Somerset, on August 6, 1877. After receiving his early education at the Ilminster Grammar School he went to Bristol, and in 1894 he qualified as a pharmacist. He did not follow this vocation long, for he was determined on a medical career, and eventually he entered St. Mary's Hospital medical school, where, after gaining several prizes, he qualified in 1904. Then followed a period of resident appointments at St. Mary's Hospital. He became keen on surgery, and was soon appointed surgical registrar to the Wigan Royal Infirmary. In due course he returned to London to study for the F.R.C.S., which he took in 1914. Batten then gained further experience as medical officer to the Central London Sick Asylum, Cleveland Street, and later at the West End Hospital for Nervous Diseases. There he came under the influence of the late Mr. E. Laming Evans: this association undoubtedly kindled his interest in orthopaedic surgery, and his next appointment was as registrar to the Royal National Orthopaedic Hospital.

During the first world war Herbert Batten served in the R.A.M.C. as a surgical specialist, with the rank of major. He had the experience of being on board a ship which was torpedoed, but fortunately he suffered no ill effects. After the war he soon established himself in London. In 1919 he was appointed honorary orthopaedic surgeon to the Freemasons' Hospital in Fulham Road, later removed to Ravenscourt Park and renamed the Royal Masonic Hospital; in the same year another appointment, as orthopaedic surgeon to the Kent County Council at Dartford, was given to him. Then in 1920 he was appointed honorary orthopaedic surgeon to the Charing Cross Hospital, succeeding Sir Thomas Fairbank, who had transferred to King's College Hospital. Herbert Batten retired from the active staff on reaching the retiring age, but continued his work at Dartford and at the Royal Masonic Hospital until the end of the recent war. From his early days until his death he was associated with the Royal Sea Bathing Hospital, Margate, with the St. Marylebone and Western General Dispensary, and with the London Foot Hospital.

Herbert Batten was a kind and friendly man. He was utterly incapable of any harsh action, and he was always helpful, sound in advice, and justly critical. Nothing gave him more pleasure than to feel that he had been instrumental in furthering the promotion of one of his former

house-surgeons or registrars in their professional climb. Only those close to him realized this, as he was by no means demonstrative, but rather reserved. Indeed, he was a modest man; he held that papers should be published only if they contained a real contribution, and yet though his own published works were so few he practised many original methods which would have been widely applauded had he published them. He was a "terrific" worker who laboured long and diligently in the cause of his patients' welfare. Apart from his work and his home life, which in itself was full and very happy, he had outside interests, the chief being Freemasonry.

He leaves a widow and a son, who is also a member of the medical profession, and to both deep sympathy will be extended by all those whose privilege it was to have known Herbert E. Batten.—D. T.

NORMAN PATTERSON, F.R.C.S.

Mr. Norman Patterson, consulting surgeon to the aural department of the London Hospital, died suddenly at his home at Ashridge on January 16 at the age of 72.

Norman Patterson was born at Ancrum, Roxburghshire, the son of a Presbyterian minister. He was a student at Edinburgh University, where he graduated M.B., Ch.B. in 1900, going on to take the F.R.C.S. in 1905. He joined the staff of the nose and throat department of the London Hospital as registrar and demonstrator in 1912, and four years later was elected assistant surgeon to the ear, nose, and throat department. He became full surgeon in 1923 and finally consulting surgeon in December, 1942. During this period Norman Patterson held other honorary appointments in his specialty at the Royal Buckinghamshire Hospital, Aylesbury; St. Albans and Mid-Herts Hospital; Golden Square Hospital; and the Florence Nightingale Hospital. He was also consulting surgeon to the Royal School for Deaf and Dumb Children at Margate, and continued visiting the school up to the time of his death. While on a visit to the U.S.A. in 1936 he was elected a Fellow of the American Laryngological Society. At the Royal Society of Medicine he was president of the Section of Laryngology in 1946 and of the Section of Otology in 1931.

His wide experience in his specialty at the London Hospital made his opinion and judgment invaluable. He was a highly skilled operator, and at an early stage in his career he became interested in the surgical treatment of cancer of the upper respiratory tract. His proficiency in the block dissection of the glands of the neck was something not readily forgotten by those who had the privilege of witnessing it. Patterson was one of the first, if not the first, to advocate the use of surgical diathermy in excising malignant neoplasms of the upper respiratory tract, and he would never yield this field to the radiologists alone. He devised an excellent operation for excision of carcinoma of the cheek, and just before the second world war he introduced a new external approach for the radical treatment of chronic pansinusitis which has proved its worth. He was the author of articles on the pharynx and ear in *Choyce's System of Surgery*.

Norman Patterson was of rather a retiring nature, perhaps a little too much so considering his ability and achievements. Kindness to his junior colleagues, students, nursing staff, and patients was one of his outstanding characteristics. He was always willing to discuss all branches of his specialty and to give help and encouragement whenever he could. He was a lover of music and painting, and in later years he exhibited in the Medical Art Society several paintings of considerable merit. In 1908 he married Miss Winifred Dorothea Crockford, who, with a daughter, survives him. His only son died on active service —E. R. G. P.

PROFESSOR W. SCHÜFFNER

Professor Wilhelm Schüffner, whose death has just been announced from Holland, was born near Minden, in Hanover, in January, 1867. He received his medical education at the Universities of Erlangen, Würzburg, and Munich, and at the age of 30 became chief medical officer to large estates in eastern Sumatra. It was during this period that he first described in 1899 the stippling of the red cells infected with *Plasmodium vivax*, the condition now known throughout the English-speaking world as "Schüffner's dots." In 1916 he became medical adviser to the Government of the Dutch East Indies and had much to do with improving health conditions in Java and Sumatra. From 1922 to 1937 he was professor of tropical hygiene at the Royal Colonial Institute in Amsterdam, and from 1924 to 1937 he was medical director of the Institute. From 1937 until 1944 he continued to act as director of the Schüffner Laboratories of the Institute.

Schüffner's contributions to tropical medicine were of outstanding importance. As early as 1900 he had recognized the value of oil of chenopodium in the treatment of ankylostomiasis. On his return to Holland he became specially interested in leptospirosis, which he had first encountered in the East. He was a world authority on this subject, and first showed the importance of the agglutination test in diagnosis. Many of his communications on this and other subjects were published in English. It was largely as a result of his work and his address to the Royal Society of Tropical Medicine and Hygiene in 1934 that leptospirosis was recognized as a common and important disease of man and animals. Many will look back with pleasure to the kindly, generous man they knew before the Nazi plague spread over Europe. Few of those who attended the International Congress of Tropical Medicine at Amsterdam in September, 1938, will soon forget his anguish at the gathering storm which was so soon to overwhelm his own and his adopted country.—G. M. F.

Dr. CHARLES GUTHERLESS MARTIN, a member of the Council of the B.M.A. since 1945, died suddenly on January 14 at his home in London. Dr. Martin was a student at St. Bartholomew's Hospital, where he qualified in 1921. He was deputy medical officer to the Port of London authority, and for many years a member of the medical advisory committee of the Royal Masonic Hospital. Dr. Martin had been active in the affairs of the B.M.A. long before his election in 1938 as chairman of the Lambeth and Southwark Division. From 1939 until 1947 he was the honorary secretary of the Metropolitan Counties Branch, of which he was elected president as recently as June of last year. As a member of Council he had been active on the Committee on Nursing, the Building Committee, and other central committees. He served also on the Medical Planning Commission, and he had been a member of the Local Medical Committee in London for nearly twenty years. He was treasurer of this committee from 1939 until his death, and latterly he had served on the London Executive Council and its Medical Services Committee.

Dr. E. A. Gregg writes: The news of the sudden death of Charles Martin came as a profound shock to all who had been intimately associated with him for many years. He gave himself unstintingly to the duties of many important offices in his own Division, in the Metropolitan Branch Council, and on the Council of the Association. All his friends were delighted when quite recently he was elected president of the Metropolitan Counties Branch. He was quiet, unassuming, and indefatigable in the discharge of all his duties. Steadfast loyalty to his

profession and to the B.M.A. characterized all his actions. Though for a long time his health had not been good he showed dogged persistence in his devotion to the work he did for his colleagues right up to the last day of his life. He was a prominent member of many Freemason lodges and chapters, and was well known and much loved in the higher ranks of the order, to which he was devotedly attached. He will be sadly missed in these circles. A staunch and loyal friend, he had a quick sense of humour. His name will be cherished in affectionate memory by all whose privilege it was to know him well.

Dr. FREDERICK WILLIAM WARREN died at Maidstone on December 9, 1949, at the age of 79. Dr. Warren studied medicine in Dublin and qualified in 1911. He was awarded the Carmichael gold medal for operative surgery and silver medals in midwifery, histology, and forensic medicine. He returned to England in 1916 and was in practice in Dulwich. He moved to Maidstone about thirty years ago, where he built up a large practice and in due course took his four sons into partnership. He carried on his work until a few months ago.

C. K. B. writes: There must be many families in and around Maidstone who mourn not only the death of the "Old Doctor," but the passing too of a counsellor and friend. I first knew Dr. Frederick William Warren when I was a child, when various childish ailments were completely overshadowed by the glories of "the doctor's Christmas Party." We all adored him, and I am perfectly sure no child of my generation ever shed tears when Dr. Warren was around. As I grew older it was probably his example more than anything else which directed my steps into medicine, and he was there to rejoice with me when I qualified. He certainly stands as one of the finest of the great old school of the real family doctor. He knew all his families of all sorts and conditions, and what the children and grandchildren were doing—all about that urticaria you had when you were 6 because of pinching gooseberries, of the pneumonia you had at 20 and which base was involved. He preferred dispensing his own medicine, and a rare hand he was at the job. He kept abreast of the times and made use of modern chemotherapy, but certainly preferred to put up a favourite mixture and finish it off with snow-white paper, perfectly folded, with a bright blob of sealing wax at each end. We can but mourn the loss of a grand old man, and extend to his widow, daughters, and four sons, who have followed in his footsteps, our most sincere sympathy.

Dr. NATHANIEL CAINE, who died at his home in New Ferry, Cheshire, on December 12, 1949, at the age of 78, was the eldest son of the late Nathaniel Caine, of Spital, Bromborough, Cheshire. He was educated privately and at St. Andrews and Edinburgh Universities, graduating M.B., C.M. in 1895 and proceeding M.D. four years later. After a period as house-surgeon, first at Oldham Infirmary and later at the Children's Infirmary, Liverpool, he went into partnership in New Ferry, Cheshire, and there he continued in general practice for nearly fifty years. Dr. Caine was the first part-time medical officer appointed by Lever Brothers, Limited, for their hospital at Port Sunlight. He was also medical officer to the Post Office and the police for many years, and was chairman of the Birkenhead and Wallasey district medical boards throughout both world wars. He always took an active part in the work of the St. John Ambulance Brigade, and in 1944 was appointed an officer of the Order of St. John of Jerusalem. Since 1920 he had served as a J.P. for the County of Cheshire. In his own neighbourhood Dr. Caine was universally respected not only for his professional skill but for his wisdom and kindliness, though he was the most modest and self-effacing of men. His death will be mourned by all those for whom he worked and all those who worked with him. He leaves a widow and two married daughters.

Dr. SELWYN GURNEY CHAMPION, a world-famous student of proverbial folklore, died at his home in Framfield on December 13, 1949. He was born at Burgess Hill in 1874, qualified in Edinburgh in 1897, and proceeded M.D. in 1902, his thesis being highly commended. A keen athlete, he played rugger for Edinburgh University and rowed in the University crew. After thirty-two years of general practice in Bournemouth, where he held a hospital appointment as assistant physician, he retired to Burgess Hill and later moved to Framfield. When still a boy Champion became attracted to proverbs and remembered all his life that it was the saying, "A rolling stone gathers no moss," that first intrigued him. He became a great collector and master of proverbs and devoted his years of leisure, up to the last day, to this fascinating study. His two outstanding works are *The Eleven Religions and their Proverbial Lore* (Routledge, 1942) and the *Racial Proverbs* (Routledge, 1938). In this monumental work, the only one of its kind, 26,000 proverbs have been gathered from every part of the world and grouped together according to their country of origin. This collection proves, as Champion states in his introduction, that proverbial wisdom is exactly the same all the world over, differing only in the rendering. Men are known by their companions, and Dr. Champion's communion with the quintessence of human philosophy became him happily. He was a delightful friend, and truly lovable.—H. P. S.

Dr. LANCELOT GERARD BOURDILLON died at his home in Goring-on-Thames on January 4 at the age of 61. Dr. Bourdillon was born in South Africa, and educated at Tonbridge and at St. Thomas's Hospital, qualifying in 1912. In the Balkan war he went to Turkey with the St. Thomas's Mission, and he contracted typhoid fever and was laid up in Constantinople for some weeks. At the beginning of the 1914–18 war he joined the 1st Field Ambulance and went to France with the 1st Division, serving abroad right through the war. As a regimental medical officer he was awarded the D.S.O., the M.C. and bar, and the Croix de Guerre, and he was mentioned six times in dispatches. In 1923 he left the R.A.M.C. with the rank of major, and went back to St. Thomas's Hospital, taking the D.P.H. in 1923 and graduating M.B., B.S. in the following year. Before settling in general practice in Goring in 1926 Dr. Bourdillon served for a time as assistant medical officer of health for Lindsey, Lincolnshire. In 1939 he was called up again, and served right through the war, being appointed A.D.M.S. Gambia and later A.D.M.S. Suez Canal Zone. In 1945 he again retired from the R.A.M.C. with the rank of full colonel and came back to Goring, where he practised until his death, following a long illness. Lancelot Bourdillon was loved and respected by his patients and all his colleagues. He was a past president of the Reading Pathological Society, and had been elected chairman of the Reading Division of the B.M.A. as recently as May of last year. He also served as chairman of the Goring and District British Legion. He is survived by his widow, two daughters, and a son, who is at present a medical student at St. Thomas's Hospital.

Dr. Charles Barber writes: ALEXANDER GIBSON (January 21, p. 193) and myself were friends for fifty years, dating from our first term together at Oxford. There we pursued the same studies, attended the same lectures, dissecting-rooms, and laboratories, and took the same examinations, culminating in the Final Schools in Physiology at the same time, and we emerged next to each other on the List (he was one above me). He was always distinguished by his unaffected modesty, honesty, integrity, and singleness of purpose—shy and very likeable withal, and with a dry sense of humour. All these qualities he kept unchanged to the end. On returning from many years abroad I found the same A. G. G. as of old, quite unchanged despite his attainments, the just fruition of his steady work, and his very considerable reputation as a consultant. His knowledge was extensive and his clinical judgment, for which I had the greatest respect, shrewd and sound; being built on a basis of pathology and general practice, it was doubly valuable. Cruelly stricken all too soon whilst in full harness, his steadfastness stood him in good stead when for over five years he lay half paralysed and unable to talk. His cheerfulness during this dreadful period was amazing, and he enjoyed many a joke when I visited him from time to time. He was a staunch friend, a self-reliant and friendly soul, and a wise physician whom it was a privilege to know and whom we shall continue to mourn and to miss.

Medico-Legal

DOCTOR SENTENCED FOR PROCURING ABORTION

At the Cambridgeshire Assizes on January 13 Dr. Stewart Quarterman Servante, of 7, West Road, and 52, Gwydir Street, Cambridge, was sentenced to 18 months' imprisonment for unlawfully using an instrument with intent to procure a miscarriage.[1]

Mr. Lionel Jellinek, prosecuting, said that in October or November last the woman concerned found that she was pregnant and asked Dr. Servante to terminate the pregnancy. The doctor used two instruments on her. A few days later she became ill and was admitted to hospital with peritonitis. Her husband did not know she was pregnant and did not know what had happened. In evidence the woman said that the doctor had at first suggested she was a policewoman.

Cross-examined, she agreed that she had done all she could herself to end the pregnancy, but she had not used an instrument. Shown a vaginal speculum, she said that it was like one of the instruments used. She said that Dr. Servante did not sterilize the other instrument. She had been married for 13 years and had two children.

The woman's husband, a Civil Servant, said that when he told Dr. Servante what had happened the doctor was shocked and said he could not understand what had gone wrong. Towards the end of this interview the witness asked the doctor to refund part of the money his wife had paid, because he had been put to considerable expense on account of his wife's subsequent illness. The doctor replied that it was a fair request, and asked how much the husband had in mind. The husband said £25, which was half the amount his wife had paid.

At a later interview Dr. Servante told him that he had carried out similar operations and it was only the second case that had ever gone wrong. Later the doctor said that he could not return any part of the fee. He had taken a risk and people who entered into such arrangements knew quite well what they were doing. Cross-examined, the husband denied the suggestion that he had said: "You must have performed an illegal operation, and if you do not want me to go to the police you had better help me with my expenses."

Mr. Oswald Lloyd, F.R.C.S., honorary gynaecologist and obstetric surgeon to Addenbrooke's Hospital, Cambridge, said that the signs of interference he found in this case were unlikely to have been caused by the woman herself. He agreed that he would have expected a skilled surgeon to sterilize his instruments.

Dr. Servante said that this woman rang him up in November, 1949. She thought she was pregnant and asked him to examine her and confirm this. After the examination he told the woman that she was pregnant, and that in his opinion she had been interfered with, or had interfered with herself. She replied: "Yes, but it has not come off. Will you fix me up?" The doctor said he refused. He added that the woman asked how much his fee was and he said he did not want one.

Speaking of the husband's visit, Dr. Servante said that the husband accused him of having performed an illegal operation and of having been responsible for his wife's illness. The husband wanted him to give him £50. He refused to discuss the matter. Subsequently the husband asked for £100.

Cross-examining, Mr. Jellinek said that the requests for money which the doctor alleged had been made by the husband were blackmail. He asked why the doctor did not go to the police. Dr. Servante said: "In our job we do not run to the police every time." Here Mr. Justice Stable interjected: "Fifty pounds which goes up to £100, and then 'phone calls—did you not think it was about time you went to see the police then?" Dr. Servante replied: "I suppose it would have been wiser to ring up my solicitor, but I should not go to the police."

Evidence was also given by Miss Ethel Mackintosh, Dr. Servante's housekeeper, secretary, and nurse for the last 22 years. She recalled the woman's visit and said she was present during the examination by the doctor. She also described four telephone calls which had been made by the woman's husband, and she recalled one of his visits. In reply to a question, she said that she never kept the records of Dr. Servante's patients. The doctor kept his own records.

Judgment

In his summing up Mr. Justice Stable said that the issue was as simple as an issue could possibly be—one side or the other was lying. The jury was absent for 55 minutes before returning a verdict.

Addressing Dr. Servante, the Judge said: "The jury have returned a verdict of guilty in this case, and nobody knows better than you that it is the right verdict. There is no doubt that you are a man who has held high medical qualifications and held important posts, and for some reason or other your professional status declined. Having regard to the fact that there is but one charge and that there is no indication before me that you habitually carried on the practice or profession of abortionist, the sentence I pass is one of 18 months."

[1] *Cambridge Daily News*, January 13 and 14.

Universities and Colleges

UNIVERSITY OF ST. ANDREWS

The following degrees have been conferred:

M.D.—Janet E. Leng.

CH.M.—J. A. Shephard.

The following candidates have been approved at the examination indicated:

M.B., CH.B.—Christella A. Adamson, N. J. Allan, L. W. Betournay, R. F. Boucher, Helen H. H. Dickie, G. L. Ferguson, J. Harrington, Marion C. Kerr, Helen F. McLagan, H. J. Penkala.

UNIVERSITY OF GLASGOW

The following degrees were conferred on January 14:

M.D.—T. Cochrane, D. Douglas, J. D. Dow, R. M. Dykes, B. R. Hillis, Mrs. Margaret H. Kelsall (née Miller), A. A. Kirkland, J. C. W. MacFarlane.

CH.M.—D. H. Clark.

M.B., CH.B.—T. Baird, R. W. Ballantyne, Hanna R. Berg, J. M. Black, S. G. Brooks, G. R. Brown, G. T. Bryden, Isobel J. D. Butters, D. W. A. Byers, A. R. W. Climie, Margaret Cowie, G. T. Day, Jean H. Dewar, Elizabeth Fagan, Rhoda M. Fullerton, J. M. Gardner, R. E. C. Gibson, A. Gillie, K. W. M. Grossart, Frances M. W. Hamilton, J. R. Hood, D. Hutchison, G. E. A. Izuora, D. R. S. Leslie, Morven E. Macaulay, H. McG. McBryde, D. McCue, J. McEwan, M. MacA. MacKay, Anne M. McKechnie, I. M. Maclean, A. McQueen, J. B. Marshall, A. B. Miller, T. R. D. Moffat, A. W. Mollison, A. E. W. Morton, Isobel M. Muir, Mary C. W. Neilson, D. A. Player, L. G. Samuel, S. P. Smith, J. Steel, H. Steingold, Sarah F. Stevenson, D. Sturrock, W. M. Walker, J. R. Welsh, W. D. Wilson.

UNIVERSITY OF LONDON

The bequest of the late Mrs. Jessie Florence Clifford for the establishment of one entrance scholarship in medicine to be called the Ken Clifford Scholarship and one postgraduate scholarship for research work in medicine to be called the Hazel Clifford Scholarship has been accepted and an expression of the Court's appreciation conveyed to the executors.

Professor J. M. Mackintosh has been appointed delegate of the University at the Health Congress of the Royal Sanitary Institute to be held at Eastbourne from April 24 to 28, and Sir Stewart Duke-Elder delegate at the sixteenth International Congress of Ophthalmology to be held in London from July 17 to 21.

Professor J. M. Mackintosh has been appointed Heath Clark Lecturer for 1951 and has been invited to deliver a course of five lectures on "Trends in Public Health in the Twentieth Century."

The following have been appointed or nominated for appointment or reappointment as representatives of the University on the governing bodies indicated in parentheses: Sir Archibald Gray (General Medical Council and School of Pharmacy); Mr. J. B. Hunter (School of Pharmacy).

The following candidates have been approved at the examinations indicated:

M.D.—*Branch I (Medicine):* A. W. Anderson, H. J. G. Bloom, J. P. Bound, J. P. Bradshaw, F. S. W. Brimblecombe, C. J. M. Clark (*Mark of Distinction*), R. A. Craig, D. Davies, A. P. Fletcher, R. M. Hardisty, J. M. Hill, A. F. Huston, R. J. Isaac, A. D. M. Jackson, H. E. M. Kay, E. C. B. S. Keat, L. G. Kiloh, A. Knudsen, M. Leivers, B. S. Lush, A. Nimalasuria, W. S Peart, E. Sanders, D. G. Sheffield, V. H. Springett (*University Medal*), I. McD. G. Stewart, Cecily M. Tinker, D. A. H. Trythall, J. S. Watson, P. Ll. Watts, J. C. P. Weber, Elizabeth Williamson. *Branch II (Pathology):* G. T. Allen, W. E. D. Evans, E. Geiringer, E. J. Harries, E. Levy, E. Neumark, J. A. Nissim (*University Medal*), S. Shaw, J. C. Sherris, P. Story. *Branch III (Psychological Medicine):* E. J. Anthony (*University Medal*), R. A. Blair. *Branch IV (Midwifery and Diseases of Women):* C. J. Champ, C. T. F. Ealand. *Branch V (Hygiene):* H. Binysh, W. A. Karunaratne, J. C. McDonald.

UNIVERSITY OF MANCHESTER

The following candidates have been approved at the examinations indicated:

FINAL M.B., CH.B.—*Old Regulations:* Margaret Bolland, P. W. Carnie, D. G. Cottrell, P. A. Ellis, P. Feingold, J. E. Glover, G. L. Glynne, Barbara C. Hanson, J. Jackson, H. A. Mitchell, K. D. Pinson, J. A. Platt, C. W. M. Pratt, Margaret E. Reynolds, Audrey Seddon, I. Sieff, Audrey J. Telford, C. A. Unsworth, [1]Margaret D. Walsh, Alwyn Wilkinson, B. A. Wolfenden. *New Regulations: Part I (Hygiene and Preventive Medicine and Forensic Medicine).*—W. de C. Baker, Margaret Bentley, [2]H. V. W. Coupe, [2]P. Fulton, A. Hyman, S. G. Jeffs, J. H. Latchford, Jean McCracken, [2]J. V. Parry, M. L. Reynolds, D. W. Sumner, [2]S. E. Sutton, Beatrice M. Swift, Olive M. Thomas, [1]B. Ward, G. R. Whittaker. *Part II (Obstetrics, Gynaecology, and Paediatrics):* B. L. Alexander, W. de C. Baker, Constance M. Bevan, Flora M. Bisset-Smith, S. M. Broman, P. Burgess, J. C. Canney, Muriel D. Carr, G. Clarke, Barbara M. Couldwell, E. J. Epstein, J. D. Evans, M. C. Flasher, M. Fox, G. Garrett, G. R. Gates, F. G. Hardman, R. Hinchcliffe, G. Howitt, T. R. Hunter, W. Kerns, [1]B. J. Leonard, M. A. Lerner, W. H. Lyle, Maria R. Mackay, B. E. Marks, A. W. Moule, Nancy Parkin, R. Price, G. V. Purnell, K. L. Purnell, J. Robinson, [1]Dora M. J. Rosbotham, R. Schofield, H. Selcon, S. Shubert, S. Stead, Hazel W. Symon, Margaret R. Walley, G. M. Watson, Sheila M. E. West, [1]A. M. Womack.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—H. J. B. Miller, P. H. Mitchell.

[1]Distinction in Hygiene and Preventive Medicine. [2]Distinction in Forensic Medicine.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

M.D.—G. Ansell, J. L. Lanceley, A. G. H. Menzies, J. S. Porterfield, E. Walker, C. J. Williams.

M.CH.ORTH.—M. A. Abdallah, G. Y. Akrawi, C. E. L. Allen, F. G. Day, R. Iskander, E. A. Jones, W. B. Law, R. W. McGlynn, P. M. McLean, K. L. Marks, H. B. C. Milsom, N. Rosenzweig, N. J. Royle, W. H. Scrase, R. G. Townsend, A. W. J. Watts.

M.RAD.—A. J. H. Henning.

FINAL M.B., CH.B.—*Part III (Old Regulations):* D. J. Adams, Dorothy M. Broadhurst, Lily I. Chesham, A. J. Cunningham, Betsy E. Davies, E. J. Davies, J. S. Endbinder, C. Griffith, J. G. Kay, E. W. Lewis, E. S. Lovgreen, B. J. Maxwell, G. K. S. Roberts. *Passed in separate subjects:* P. H. Grace (Medicine, Surgery), G. Jones (Surgery, Obstetrics and Gynaecology), H. Riad (Medicine, Obstetrics and Gynaecology). *Part II (Old Regulations):* Sheila R. Clarke, Betty E. Hodgkinson, J. C. Holden, A. W. G. Housby, P. F. Knight, Jean M. Naylor, Jean A. Raffle, T. D. Reilly, Gwendoline D. Salter, R. W. Saul, J. S. V. Surman, Sheila M. Ward, H. Wilson.

D.P.H.—*Part I:* L. N. Gould, A. Haji Alias, J. T. O'Sullivan, H. N. Singh, L. S. Stephens.

CERTIFICATE IN PUBLIC HEALTH.—Joyce M. Havelock, Mair Humphreys, J. J. Montague, Enid Rees.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

The following lectures will be delivered at the College (Lincoln's Inn Fields, London, W.C.) at 5 p.m. on each day: Thursday, February 2, Otolaryngology Lecture by Professor W. Barnard, "The Contribution of Pathology to the Diagnosis of Tumours in Otolaryngology"; Thursday, February 9, Hunterian Lecture by Professor Denis Browne, "Congenital Deformities of the Urethra, Vagina, and Anus"; Thursday, February 16, Hunterian Lecture by Professor J. E. A. O'Connell, "A Review of 500 Surgically Treated Cases of Lumbar Intervertebral Disk Protrusion, with Especial Reference to the Late Results of Operation"; Tuesday, February 21, Hunterian Lecture by Professor J. E. Piercy, "Factors Contributing to Safety in Surgery of the Thyroid"; Thursday, February 23, Hunterian Lecture by Professor H. L. M. Roualle, "Malignant Disease of Thyroid Gland"; Tuesday, February 28, Hunterian Lecture by Professor E. M. Evans, "Fractures of the Radius and Ulna."

The lectures are open to those attending courses in the College and also to all other medical practitioners, dental surgeons, and advanced students.

The Buckston Browne Annual Dinner of Fellows and Members will be held at the College (Lincoln's Inn Fields, London, W.C.) on Tuesday, February 14, at 7.30 for 8 p.m.

At a meeting of the Council of the College, held on January 12, with Sir Cecil Wakeley, President, in the chair, it was announced that Sir Max Page would be the Hunterian Orator for 1951; Mr. William Doolin the Thomas Vicary Lecturer for 1950; and Professor P. D. Wilson, Robert Jones Lecturer for 1950.

Diplomas in Tropical Medicine and Hygiene, in Psychological Medicine, in Laryngology and Otology, in Medical Radiodiagnosis, in Medical Radiotherapy, and in Industrial Health were granted jointly with the Royal College of Physicians of London to the following successful candidates:

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—W. E. Barnes, A. K. Basu, D. E. Boye-Johnson, C. F. Egan, M. M. Lewis, C. P. Nanavati, H. N. Singh, S. C. Ferguson, D. W. Quantrill.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—L. D. Gardner, A. Gillis, D. Lewis, W. V. Livingston, I. H. Martin, H. F. Osmond, L. Sohn.

DIPLOMA IN LARYNGOLOGY AND OTOLOGY.—M. A. Abul Ela, N. Ahmad, A. J. E. Blayney, C. C. Corbett, P. R. Das Gupta, W. R. Denny, G. Freeman, W. G. L. Hood, D. G. Jones, J. I. Kelly, P. J. O. McCullen, J. K. Madan, W. A. Malik, H. M. Parsons, C. H. H. Robertson, J. R. Ryan, D. V. Sethi, S. Silbermann, T. Tenderenda, J. D. Trethowan, B. C. Devane.

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—J. Ainsworth, H. S. Ali, A. H. Ansári, E. B. Bradbury, T. D. Brick, J. B. Chetwynd, W. R. Cole, S. Davis, W. H. Dempster, J. R. Dow, D. Dowera, E. P. G. H. du Boulay, P. K. Dutt, E. R Edmunds, J. T. Furnival, D. McC. Gregg, C. I. Griffiths, H. J. Hagger, G. K. E. Inman, N. R. Jefferson, J. V. Kent, A. H. McCallum, A. N. K. Menon, G. Osborne, M. Ramzan, K. G. Reynolds, P. W. E. Sheldon, B. S. H. Storr, J. Sutcliffe, D. K. M. Toye, K. S. Warang, Krystyna Wowkonowicz.

DIPLOMA IN MEDICAL RADIOTHERAPY.—W. R. Argument, R. J. Dickson, A. M. Gandhi, Helen C. Hodges, J. Kinsella, W. Kulke, M. Marlborough, J. J. Nickson, R. J. Walton.

DIPLOMA IN INDUSTRIAL HEALTH.—M. M. Abdel-Latif, D. K. Cowan, A. David, A. W. Gardner, R. F. Guymer, E. A. W. Marien, J. M. Muir, G. H. G. Southwell-Sander.

The following hospitals were recognized under paragraph 23 of the F.R.C.S. regulations: Horton General Hospital, Banbury (senior house-surgeon and junior house-surgeon, for six months); Joyce Green River Hospitals, Dartford (surgical registrar, senior house-surgeon, two house-surgeons); Royal Gwent Hospital, Newport (resident orthopaedic officer, house-surgeon to orthopaedic department, for six months only); Birch Hill Hospital, Rochdale (two house-surgeons, resident surgical officer, one orthopaedic registrar, for six months only); Rochdale Infirmary (resident casualty officer, resident surgical officer, house-surgeon, for six months only).

It was decided that in future the annual meeting of Fellows and Members would be held on the day preceding the second Thursday in December and that on the same day there should be one of the statutory lectures, the monthly dinner, a "view day" in the various departments of the College, and the annual show of recent additions to the museum.

The Services

DEATHS IN THE SERVICES

Major-General Sir MICHAEL WILLIAM RUSSELL, who died at his home at Crowborough, Sussex, on December 6 at the age of 89, was Deputy Director-General of the Army Medical Services during the 1914–18 war. He was born on June 23, 1860, and received his medical education at the Middlesex Hospital, qualifying in 1881. He joined the Army Medical Service four years later and went out almost immediately to the Sudan. He took part in the engagement at Giniss, and in 1890 was a member of the Zhob valley and Kidderzai expeditions under Sir George White. For his services in the South African war he received the Queen's medal with three clasps and the King's medal with two clasps, and was mentioned in dispatches. He was also at this time promoted lieutenant-colonel, and subsequently he joined the medical directorate at the War Office at first as D.A.D.-G., continuing in the directorate until the end of his career. Major-General Russell was made a C.B. in 1916 and a K.C.M.G. in 1918 just after his retirement. He married in 1892 Mary, daughter of the late Colonel C. H. Plowden, who died in 1944.

No. 1

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended January 7.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county) (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1950 (a)	(b)	(c)	(d)	(e)	1949 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Meningococcal infection	39	5	21	—	—	28	3	18	2	—
Deaths		1	1				2	—		
Diphtheria	75	12	23	4	6	142	18	26	5	2
Deaths	—	—	—	—	—	3	—	—	—	—
Dysentery	199	17	54	—	—	53	9	39	—	—
Deaths					—				—	—
Encephalitis, acute	4	—	—	—	—	—	—	—	—	—
Deaths		—					2			
Erysipelas			34	13	7			35	9	2
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				14					36	
Deaths	27	1	7	8	1	39	5	8	2	5
Measles*	2,337	43	12	85	219	11,121	294	41	81	52
Deaths†			—	—	—			—	1	—
Ophthalmia neonatorum	46	2	12	—	3	48	5	16	—	—
Deaths										
Paratyphoid fever	3	1	—	—	—	3	1	—	1(B)	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	1,120	72	19	4	17	1,050	59	6	6	4
Deaths (from influenza)‡	52	7	3	—	—	29	3	2	—	—
Pneumonia, primary			408	¶				373	54	
Deaths	299	66		21	6	330	62		14	11
Poliomyelitis, acute	54	1	1	5	1	23	—	5	3	—
Deaths§	10	1		1		2	—			
Puerperal fever		—	7		—		—	9		—
Deaths										
Puerperal pyrexia‖	97	5	6	—	—	66	4	5	—	—
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,798	122	255	89	178	1,125	54	245	109	42
Deaths†			—	—	—			—	1	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths					—				—	—
Typhoid fever	28	1	—	3	—	7	1	—	2	—
Deaths	—	—	—		—	2	1	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,379	61	147	41	50	2,015	133	50	70	15
Deaths	3	—	—	—	1	10	—	2	1	1
Deaths (0–1 year)	289	46	65	29	10	359	44	56	30	15
Deaths (excluding stillbirths)	5,631	935	720	214	137	6,362	1047	743	242	121
Annual death rate (per 1,000 persons living)			14·4					15·0	15·1	
Live births	7,364	1266	943	391	255	7,253	1172	898	379	280
Annual rate per 1,000 persons living			18·9					18·1	23·7	
Stillbirths	180	31	28			186	31	23		
Rate per 1,000 total births (including stillborn)			29					25		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* there were increases in the notifications of whooping-cough 361, measles 359, and acute pneumonia 278, with decreases in the incidence of scarlet fever 529 and diphtheria 27.

The largest rises in the notifications of whooping-cough were 43 in Warwickshire and 30 in Lancashire. The largest variations in the incidence of measles were increases in Suffolk 106 and Lancashire 69, and decreases in Durham 65 and Northamptonshire 34.

The incidence of scarlet fever fell in most areas; the largest decreases were Lancashire 137 and Cheshire 75. Notifications of diphtheria decreased in Lancashire 13 and Warwickshire 6. The largest increases in the incidence of acute pneumonia were: Yorkshire West Riding 55, Middlesex 39, and Warwickshire 36; the largest decrease was 29 in Lancashire.

Only 7 cases of dysentery were notified in Newcastle-upon-Tyne C.B., where 69 cases were notified in the preceding week. An outbreak of dysentery, with 86 notifications, was reported from Staffordshire, Smethwick C.B.; 20 cases had been notified in this town during the preceding fortnight. The other important centres of dysentery were London 17 (Islington 7); Glamorganshire 14 (Penarth U.D. 8); Yorkshire West Riding 12 (Barnsley C.B. 10); Durham 11; and Lancashire 10. Of the 28 cases of typhoid fever 20 were notified in the Port Health District of London.

In *Scotland* increases were recorded in the notifications of whooping-cough 87 and acute primary pneumonia 46. Notifications of dysentery were 59 fewer than in the preceding week; the chief centres of dysentery during the week were Glasgow 28 and Ayr county 16.

In *Eire* an increase of 29 was recorded in the notifications of measles and a decrease of 22 in the incidence of scarlet fever. Only 14 cases of diarrhoea and enteritis were notified, including 6 from Dublin C.B. A further 47 cases of measles were notified in Waterford, Carrick-on-Suir No. 2 R.D.

In *Northern Ireland* there was an increase of 74 in the notifications of measles, with a decrease of 18 in the incidence of scarlet fever. The largest increases in the incidence of measles were Belfast C.B. 28 and Antrim county 36.

Infectious Diseases During 1949

The incidence of diphtheria during the year showed a further large fall, and the uncorrected notifications were only one-fifth of the number recorded five years earlier and less than one-twelfth of the notifications in 1937 and 1938. Only 52 cases were notified during the thirty-fourth week of 1949 compared with 788 and 815, the lowest weekly totals during 1937 and 1938.

The biennial period which was apparent during the first years of measles notifications has not appeared during the last four years, and the annual totals have been practically constant.

Notifications of cerebrospinal fever were the lowest for the past five years. Enteric fevers were more prevalent than in the two preceding years. The epidemic of acute poliomyelitis produced about two-thirds the number of notifications recorded in 1947, and notifications continued at about eight times the old endemic level.

The number of deaths attributed to influenza in the great towns was the largest for the past five years, but the total was considerably below some of the immediately preceding years. In 1937, 1940, and 1943, deaths from influenza numbered 8,341, 5,510, and 6,280.

	Number of Notifications 1945	1946	1947	1948	1949
Scarlet fever	74,392	57,614	60,524	75,460	71,753
Measles	443,002	154,826	399,461	396,841	384,361
Whooping-cough	62,022	92,028	94,241	145,878	102,516
Diphtheria	25,059	18,156	10,528	7,903	4,929
Acute pneumonia	34,059	36,106	34,348	31,096	34,624
Cerebrospinal fever	2,691	2,627	3,147	1,971	1,586
Acute poliomyelitis	799	703	8,592	2,017	6,334
Dysentery	16,533	8,441	4,179	5,587	4,819
Typhoid and paratyphoid fever	679	1,367	880	873	1,138
Influenza. Deaths in the great towns	1,307	2,629	1,774	610	3,091

Health of London, 1949

The provisional birth rate was 16.9, the lowest for the past four years. Infant mortality at 28 per 1,000 live births was the lowest rate ever recorded in London. The death rate was 11.9 and was 0.8 above the rate for 1948. Deaths attributed to poliomyelitis numbered 55. Deaths from diphtheria numbered 7 compared with the pre-war level of 250. There were 235 persons killed in road accidents.

Week Ending January 14

Notifications of infectious diseases in England and Wales during the week included : scarlet fever 1,758, whooping-cough 1,535, diphtheria 81, measles 2,318, acute pneumonia 991, acute poliomyelitis 50, dysentery 154, typhoid fever 8.

Medical News

President of British Council

Sir Henry Dale, O.M., F.R.S., has been elected President of the British Council by its Executive Committee in succession to Lord Riverdale, who has resigned for private reasons. Sir Henry Dale was a member of the Council's Executive Committee from 1943 to 1949, and chairman of its Science Advisory Committee from 1942 to 1949. He has been President of the Royal Society, the British Association, and the Royal Society of Medicine, and shared the Nobel Prize for medicine and physiology with Professor Otto Loewi in 1936.

Leverhulme Research Fellowships

Application is invited for Leverhulme fellowships and grants in aid of research. They are intended for senior workers prevented by routine duties or pressure of other work from carrying out research. They are limited to British-born subjects normally resident in the United Kingdom ; in exceptional circumstances the trustees may waive the condition as to residence. The trustees will also consider applications from groups of workers engaged on co-operative programmes of research, particularly from those engaged on long-term programmes or in institutions in which the normal facilities for research have been curtailed by the war. The duration of the awards will not normally be for more than two years or less than three months, and the amount will depend on the nature of the research and the circumstances of the applicant. Forms of application may be obtained from the Secretary, Dr. L. Haden Guest, Leverhulme Research Fellowships, 7, Bedford Row, London, W.C.1. Applications must be received on or before March 1, 1950. Awards will be announced in July and will date from September 1, 1950.

Exhibition of Psychopathological Art

An exhibition of psychopathological art is to be held at the International Congress of Psychiatry in Paris on September 18 to 27. Those interested in showing exhibits are invited to communicate with Dr. E. Cunningham Dax, Netherne Hospital, Coulsdon, Surrey, preferably before the end of February.

Grants for Study in U.S.A.

A limited number of Smith-Mundt grants are available to university teaching staff or those of equivalent academic status in other institutions, and to senior research workers, who wish to visit the U.S.A. for study, research, or lecturing. Applicants must be citizens of the United Kingdom, and must be affiliated to an American institution of higher learning. Candidates may apply if they have not yet concluded affiliation but are virtually certain to do so. Candidates in the research group must spend at least three months in the U.S.A., and lecturers visiting American universities at least six months or one semester. Grants are also made to cover the return fare. Those wishing to apply should write immediately to the United States Educational Commission in the United Kingdom, 55, Upper Brook Street, London, W.1. Application forms obtained from that address must be returned to it before February 18.

David Anderson-Berry Prize

A David Anderson-Berry silver-gilt medal, together with a sum of money amounting to about £100, will be awarded during 1950 by the Royal Society of Edinburgh to the person who, in the opinion of the council, has recently produced the best work on the therapeutic effect of *x* rays on human diseases. Applications for the prize are invited. They may be based on both published and unpublished work and should be accompanied by copies of the relevant papers, and must reach the General Secretary, Royal Society of Edinburgh, 22, George Street, Edinburgh, 2, by March 31.

King Edward's Hospital Fund

His Majesty the King has sent an annual subscription of £1,000 for 1950 to King Edward's Hospital Fund for London. The Fund has also received a further instalment of £100,000 from the Nuffield Trust for the Special Areas. In founding this trust Lord Nuffield provided that any sums that might be available by way of repayment of loans or otherwise from the trust should pass to King Edward's Hospital Fund. A total sum of £1,250,000 has now been received.

German Periodical

A well-known German weekly, *Die medizinische Welt*, ceased publication in 1944 after a successful life of nearly 20 years. It has now reappeared as *Die neue medizinische Welt*, with Professor Volhard, of Frankfurt, as chief editor. Its aims are stated to be the dissemination of essentially practical information for general practitioners and specialists, the provision of space for articles based on observations by general practitioners, and the discussion, usually by two authorities, of questions sent in by readers.

Medical Artists' Association

The Medical Artists' Association of Great Britain has been established to " raise the standard of medical art " and to " safeguard the professional status of qualified medical artists." Sir James Learmonth is president of the M.A.A. and Mr. D. H. Tompsett, Ph.D., the chairman, to whom inquiries may be sent at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2. A letter setting forth the aims and objects of the Medical Artists' Association appears in this week's correspondence columns.

Wills

Dr. Geoffrey Seccombe-Hett, formerly consulting surgeon to the Royal Ear Hospital and to University College Hospital, left £797. Dr. Frederick John McKettrick, of Danbury, Essex, left £14,609 ; Dr. Duncan Matheson Mackay, of Campbeltown, Argyll, £21,506 ; and Dr. Urban Marks, of Bishopston, Glam. £22,469.

COMING EVENTS

Philosophy of Human Nature

Mr. Karl Britton, senior lecturer in philosophy at University College of Swansea, will deliver a course of four lectures on " The Philosophy of Human Nature " at the Royal Institute of Philosophy, University Hall, 14, Gordon Square, London, W.C., on Fridays, January 27 and February 3, 10, and 17, at 5.15 p.m. Admission to the lectures is free.

Registrars Association, South-eastern Region, Scotland

All registrars in the South-eastern Region, Scotland, are invited to attend the general meeting of the Registrars Association at B.M.A. Scottish House, 7, Drumsheugh Gardens, Edinburgh, on Wednesday, February 1, at 8 p.m. Amongst other business, three representatives will be elected to the Central Council of the Registrars Group of the B.M.A.

Contraceptive Technique

A lecture and demonstration (on living models) on contraceptive technique will be given by Dr. Marie C. Stopes and Dr. Beddow Bayly at the Mothers' Clinic, 108, Whitfield Street, London, W., on Thursday, February 2, at 2.30 p.m. Tickets must be obtained in advance, as space is limited.

People and Planning

The British Social Hygiene Council and the Town and Country Planning Association will hold a joint conference on "People and Planning" on Thursday and Friday, February 2 and 3, at the Planning Centre, 28, King Street, London, W.C.2. The report of the Royal Commission on Population will be considered. The speakers include Dr. C. P. Blacker. Information may be obtained from the British Social Hygiene Council, Tavistock House North, Tavistock Square, London, W.C.1. Tickets are 10s. for members of either association, and 15s. for non-members.

SOCIETIES AND LECTURES

Friday

ROYAL INSTITUTE OF PHILOSOPHY, University Hall, 14, Gordon Square, London, W.C.—January 27, 5.15 p.m., "*The Philosophy of Human Nature and the Science of Human Nature*," by Mr. Karl Britton (University College of Swansea).

Monday

UNIVERSITY COLLEGE, Gower Street, London, W.C.—January 30, 4.30 p.m., "*Biochemistry of Carotenoids*," by Professor R. A. Morton.

Tuesday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—January 31, 5 p.m., "*Histopathology of the Skin*," by Dr. I. Muende.

PADDINGTON MEDICAL SOCIETY.—At St. Mary's Hospital, Paddington, London, W., January 31, 9 p.m., "*Treatment of Obesity*," by Dr. J. Lieber.

Wednesday

HARVEIAN SOCIETY OF LONDON.—At 26, Portland Place, London, W., February 1, 8.15 p.m., "*Current Thoughts on Corneal Graft Surgery*," by Mr. B. W. Rycroft.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—February 1, 4.30 p.m., lecture-demonstration for postgraduates by Dr. E. Stengel.

KENT PAEDIATRIC SOCIETY.—At Court Leas Approved School, Godstone, Surrey, February 1, 2.30 p.m., meeting.

SOCIETY OF PUBLIC ANALYSTS.—At Burlington House, Piccadilly, London, W, February 1, 7 p.m., "*Modern Methods of Moisture Determination*," papers by Messrs. A. G. Jones, B.Sc., F.R.I.C., A. T. S. Babb, B.Sc., A.R.I.C., R. W. Money, M.Sc., F.R.I.C., and C. F. M. Fryd, B.Sc., A.R.C.S., A.R.I.C., and P. R. Kiff, B.Sc. An open discussion will follow.

Thursday

DONCASTER MEDICAL SOCIETY.—At the Danum Hotel, Doncaster, February 2, Annual Dinner and Dance to be held in conjunction with Doncaster Division of B.M.A. Dinner 7.15 p.m.; dancing 9 p.m. to 1 a.m.

FACULTY OF HOMOEOPATHY.—At Royal London Homoeopathic Hospital, Great Ormond Street, London, W.C., February 2, 5.30 p.m., "*Post-influenzal Complications*," by Dr. D. M. Borland.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—February 2, 5 p.m., "*Bullous Eruptions*," by Dr. H. J. Wallace.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—February 2, 5 p.m., "*The Contribution of Pathology to the Diagnosis of Tumours in Otolaryngology*," Otolaryngology Lecture by Professor W. Barnard.

ROYAL PHOTOGRAPHIC SOCIETY: MEDICAL GROUP.—At 16, Princes Gate, London, S.W., February 2, 7 p.m., "*An Introduction to Infra-red Photography*," by Mr. J. E. Andrews, F.I.B.P.; "*Clinical Aspects of Infra-red Photography*," by Mr. Kenneth Bowes.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—February 2, 4.30 p.m., "*Neurology*," lecture-demonstration by Dr. A. Feiling.

Friday

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, Maida Vale, London, W.—At Medical School, February 3, 5 p.m., Neurological Demonstration by Dr. E. A. Blake Pritchard.

ROYAL INSTITUTE OF PHILOSOPHY, University Hall, 14, Gordon Square, London, W.C.—February 3, 5.15 p.m., "*Ways of Knowing and Kinds of Knowledge*," by Mr. Karl Britton (University College of Swansea).

UNIVERSITY COLLEGE, Gower Street, London, W.C.—February 3, 5.15 p.m., "*Aspects of Pharmacological Chemistry*," by Dr. F. Bergel.

Saturday

YORK MEDICAL SOCIETY.—At 17, Stonegate, York, February 4, 8.30 p.m., "*Cortisone (Compound E) in the Treatment of Rheumatic Diseases*," by Professor S. J. Hartfall.

APPOINTMENTS

Dr. L. W. Fitzmaurice, O.B.E., has been appointed an Official Member and Dr. A. G. Curphey, M.B.E., *M.C.*, an Unofficial Member of the Legislative Council of the Island of Jamaica.

BAIN, ALEXANDER A. N., M.B., CH.B., D.M.R., Consultant Radiologist to Northern Regional Hospital Board, Inverness.

BRITT, R. G., M.R.C.S., L.R.C.P., D.M.R.D., Senior Registrar in Radiology in Peterborough Area, East Anglian Regional Hospital Board.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*House-physicians (Junior Registrar Grade)*, V. M. Leveaux, M.D., M.R.C.P., A. D. M. Jackson, M.B., B.S., M.R.C.P., D.C.H. *House-surgeons (Junior Registrar Grade)*, H. M. Bassett, M.B., B.S., J. M. Langham, M.B., B.Ch., F.R.C.S. *Medical Registrars and Pathologists (Senior Registrar Grade)*, O. D. Fisher, M.B., B.S., M.R.C.P., D.C.H., H. R. Jolly, M.B., B.Ch., M.R.C.P., D.C.H.

HOWARD, STANLEY, M.B., CH.B., Senior Assistant Medical Officer of Health, City of Bradford.

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Consultant Non-resident Psychiatrist (Whole-time) to Rainhill Hospital*, Ilse R. Nussbaum, M.D., D.P.M. *Medical Superintendent of Rainhill Hospital*, B. Finkleman, M.Sc., M.D., D.P.M. *Consultant Anaesthetist to Hospitals in St. Helens and Warrington areas*, M. Swerdlow, M.B., Ch.B., D.A.

MACARTHUR, J. GORDON, *M.C.*, M.B., CH.B., M.R.C.P., Second Lecturer in Materia Medica, University of Glasgow, and Assistant Physician, Stobhill Hospital, Glasgow.

RAWLINSON, M. P. G., M.R.C.S., L.R.C.P., Medical Officer of Health, Stettler Health District, Alberta, Canada.

SCOULAR, GUY H., M.B., CH.B., D.P.H., Assistant Senior Medical Officer, Manchester Regional Hospital Board.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—*Consultant Surgeon in Bristol Clinical Area*, A. G. McPherson, M.Chir., F.R.C.S. *Consultant Physician in Bristol Clinical Area*, J. M. Naish, M.D., M.R.C.P. *Consultant Ear, Nose, and Throat Surgeon in Plymouth Clinical Area*, D. A. Barley, M.B., F.R.C.S., D.L.O.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Derlien.—On January 3, 1950, at St. Mary's, Manchester, to Dr. and Mrs. L. Derlien, a third son.

Howat.—On January 17, 1950, to Margaret (née Harker), wife of Dr. James Howat, Newcastle-upon-Tyne, a son.

Mayer.—On January 11, 1950, at Tunbridge Wells, to the wife of Mr. J. H. Mayer, F.R.C.S., a son.

O'Reilly.—On January 15, 1950, at the Preston Royal Infirmary, to Margaret (née Gavin) wife of Dr. Oliver O'Reilly, late of Fearmore, Rochfort Bridge, Westmeath, Eire, a son—Oliver Francis Paul.

Pattison.—On January 16, 1950, at Gloucester, to Edna, wife of Mr. G. N. Pattison, D.O., D.O.M.S., a son.

MARRIAGE

Allsopp—Cooper.—On December 24, 1949, at Ipoh, Malaya, Philip A. Allsopp, M.R.C.S., L.R.C.P., of Northwood, Middlesex, to Mary H. Cooper, L.D.S., of Dundee, Scotland.

DEATHS

Bennett.—On January 8, 1950, Robert Allan Bennett, M.D., M.R.C.P., M.R.C.S., of 39, Addison Road, London, W., late of Harley Street, London, W., aged 78.

Bourdillon.—On January 4, 1950, at his home, Stow House, Goring-on-Thames, Oxon, Lancelot Gerard Bourdillon, D.S.O., M.C., Croix de Guerre, M.B., B.S.

Brody.—On December 30, 1949, at Sheffield, Morris Benjamin Brody, M.D., D.P.M., of Graylingwell Hospital, Chichester, aged 37.

Buchanan.—On January 12, 1950, at Wallington, Surrey, Angus Buchanan, M.C., M.B., Ch.B., of Crewe, Cheshire.

Carmichael.—On January 7, 1950, at 4, Chamberlain Road, Edinburgh, Archibald Nathaniel Shirley Carmichael, M.B., C.M., F.R.C.P.Ed., aged 82.

Corsi.—On January 1, 1950, in Switzerland, Henry Corsi, M.B., F.R.C.S., of 95, Harley Street, London, W.

Edmond.—On January 8, 1950, William Square Edmond, F.R.C.S., of Womerton, All Stretton, Salop.

Farr.—On January 2, 1950, at Brighton, Valentine Francis Farr, M.B., B.S., formerly of 14, Queens Road, Kingston Hill, Surrey, aged 53.

Gibson.—On January 11, 1950, at 27, Banbury Road, Oxford, Alexander George Gibson, D.M., F.R.C.P., aged 74.

Greenfield.—On January 11, 1950, at 76, Wymington Road, Rushden, Northants, Dudley George Greenfield, M.D., F.R.C.S.

Henry.—On January 11, 1950, at the Seamen's Hospital, Greenwich, Robert Eric Henry, M.B., Ch.M., late of Sydney, New South Wales, Australia, aged 54.

Holroyde.—On January 5, 1950, at a Harrogate nursing-home, Gerald Holroyde, M.C., M.R.C.S., L.R.C.P.

Jack.—On January 8, 1950, William Andrew Morton Jack, O.B.E., M.B., B.S., Colonel, I.M.S., Ret., of Hillsleigh, Godalming, Surrey.

Jeffrey.—On January 10, 1950, at a nursing-home, Edinburgh, James Ritchie Jeffrey, M.B., C.M., of 1, Glenorchy Terrace, Edinburgh.

Last.—On January 9, 1950, at Tregunter, Bookham, Surrey, Thomas Clifford Last, M.D., late of Burnham-on-Sea.

Litchfield.—On January 10, 1950, at 14, Brighton Road, Purley, Surrey, Percy Collins Litchfield, M.C., M.R.C.S., L.R.C.P.

Livingstone.—On January 3, 1950, in London, William Livingstone, M.B., C.M., late of Seaford, Sussex, aged 88.

MacVicar.—On December 2, 1949, in Johannesburg, South Africa, Neil MacVicar, M.D., D.P.H.

Martin.—On January 14, 1950, at 134, Brixton Hill, London, S.W., Charles Gutherless Martin, M.R.C.S., L.R.C.P.

Miller.—On January 5, 1950, at Penzance, William Robert Miller, M.D., aged 85.

Milne.—On January 6, 1950, James Alexander Milne, M.D., D.P.H., of Woodford Bridge, Essex.

Murphy.—On January 6, 1950, at Whistle Crag, Middleton-in-Teesdale, Robert Walpole Murphy, O.B.E., M.D., D.P.H.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Antihistamines and the Common Cold

Q.—*According to recent reports in the lay press, antihistamine preparations have been used successfully in treating or aborting the common cold. Is this likely? If so, what is the dosage and when should it be given? Are there any contra-indications?*

A.—The reports from America that a powder containing a mixture of acetylsalicylic acid and antihistamine drugs is of value in treating or aborting the common cold have as yet not been fully substantiated and the matter is still *sub judice*. The evidence at present is quite insufficient to justify the widespread use of antihistamines for this purpose, in spite of the recent pronouncements in some of the newspapers. The writer has had a number of patients who have developed severe colds though they were at the same time taking large doses of antihistamines for the control of chronic urticaria. A considerable proportion of patients suffering from paroxysmal rhinorrhoea (allergic rhinitis) are, of course, benefited by antihistamine therapy, and it is sometimes difficult to differentiate an allergic from an infective condition of the nose, nor do we know how large a part allergy plays in the symptomatology of the common cold. In paroxysmal rhinorrhoea the dosage used should be 100 mg. "neo-antergan" three times a day, the dose being gradually increased until a satisfactory result is attained; or 25 to 50 mg. "phenergan" taken at night.

Side effects are experienced as a result of antihistamine treatment in a large proportion of cases, the most common being sleepiness, which in some patients is very pronounced when they first take the drug. Until the patient's reaction in this respect is ascertained it is unwise to prescribe these drugs for the first time before the patient undertakes work requiring mental acuity, such as driving a motor-car. The dangers of accidental overdosage in young infants were discussed in an annotation in the *Journal* of January 14 (p. 111), in which it was also pointed out that the use of these drugs in the treatment of the common cold is at present the subject of an M.R.C. trial.

Effects of Pressure on a Nerve

Q.—*What are the effects of (a) continuous and (b) intermittent mechanical pressure on a nerve? Has there been any research work done on this subject?*

A.—There is no qualitative difference between the effects of continuous and intermittent mechanical pressure on a nerve provided the intermittent pressure continues long enough on each occasion to produce any effect at all. Pressure upon a nerve operates primarily by producing ischaemia, for this leads both to degeneration of nerve fibres and to oedema of the nerve, which extends for some distance both above and below the site of the pressure. The oedema in turn contributes to the compression of the nerve fibres and thus a vicious circle is set up. Furthermore, if the pressure is not relieved fibrosis develops and the final result is a "pressure neuroma" composed of fibrous tissue with complete degeneration of the nerve. This is the pathological process which underlies a number of common lesions of nerve roots and nerve trunks, such as pressure upon a nerve root by a herniated intervertebral disk; pressure upon a spinal nerve by a narrowed intervertebral foramen; pressure upon the inner trunk of the brachial plexus by a cervical rib; neuroma of the ulnar nerve at the elbow caused by a "slipping ulnar"; compression of the median nerve in the carpal tunnel and of the lateral cutaneous nerve of the thigh in meralgia paraesthetica; and digital neuroma in Morton's metatarsalgia. A good deal of research work has been done on this subject. See, for example, the paper "Lesion in Peripheral Nerve Resulting from Compression by Spring Clip," D. Denny-Brown and C. Brenner, *Arch. Neurol. Psychiat.*, 1944, **52**, 1.

Hazards of Dichloroethylene

Q.—*A patient of mine uses dichloroethylene freely in his work and tends to get a severe headache by the afternoon. Is it likely to be the cause and, if so, is there any antidote?*

A.—It is assumed that the patient has correctly described the industrial solvent with which he works—dichloroethylene ($CHCl:CHCl$) being in less common use than trichloroethylene ($CHCl:CCl_2$). Both, however, are narcotics and are chemically akin to chloroform ($CHCl_3$). Lehmann gives the following figures of relative toxicity: trichloroethylene: dichloroethylene: chloroform = 1.7 : 1.7 : 2.2 (monophasic) and 3.8 : 12.5 : 10.8 (diphasic). "Monophasic" toxicity represents the action of the pure vapour, while "diphasic" toxicity is related to conditions of volatility and temperature and would represent ordinary usage. Severe headache for which other causes have been excluded might well be caused by exposure to dichloroethylene fumes, especially where conditions of ventilation are poor. The only antidote is fresh air, when recovery is usually rapid. The only sound prophylactic measure is for the work with dichloroethylene to be performed under conditions of localized exhaust ventilation, on the principle of the chemical fume cupboard.

Inheritance of Spina Bifida

Q.—*Is there any evidence that spina bifida is hereditary? What is the likelihood of some spinal or other abnormality occurring in any future children of parents with one child of 3 years, who has a well-marked patch of hair over his lumbo-sacral region? There are no other signs of spina bifida, and a recent x-ray picture reveals normal bone structure. Two months ago the mother had a second child who survived only a few hours because of a meningomyelocele. The only history of abnormality to be found in either family is that of a brother of the husband's father, who died at the age of six weeks with "spinal trouble."*

A.—This is a difficult question to answer. There is a tendency for spina bifida to show a familial incidence and also for other defects, for example anencephaly, to show a somewhat higher incidence amongst the sibs than in the general population. It is likely, however, that some at least of the increased familial incidence may be non-genetic, reflecting rather an unfavourable maternal environment. The chance that a further child might show a severe neurological abnormality is probably not worse than 5% if the mother is young, or 10% if she is old, say nearly 40 or more.

Copper as an Industrial Hazard

Q.—*What, if any, are the industrial hazards of copper? The process concerned consists of:* (1) *Obtaining copper oxide by electrolytic process from the metal copper. The oxide is dried, crushed, and "run" into drums. This last process is dusty and a considerable amount of dust may be suspended in the air. The men working in this are covered with the copper oxide dust.* (2) *The remains of the copper metal bars are smelted in an open crucible over a furnace and recast for further electrolytic action.*

A.—There is no evidence of the occurrence of any acute systemic poisoning due to copper metal. Copper rarely causes poisoning, although its salts are irritant and corrosive. Attempts to induce chronic copper poisoning in rabbits by feeding have been unsuccessful, although there is evidence of a considerable amount of copper storage in the liver. The occurrence of chronic copper poisoning in man has not been established. The relation of copper to haemochromatosis was investigated by Mallory, and it was thought that haemochromatosis might be due to long-continued ingestion of copper salts, but this has not been confirmed.

(1) Exposure to copper dust, copper carbonate dust, or flaked copper has been known to cause sneezing, nausea, and weakness. Schiötz describes seven cases of "copper fever" from

a paint factory in which red oxide of copper was being pulverized. Cupric oxide has been known to give rise to green coloration of the skin in workers exposed in hot environments.

With regard to (2), exposure to copper fumes or to fine spray from heated metal may give rise to metal-fume fever, the symptoms of which are rigor, fever, muscular pains, and headache occurring a few hours after exposure. Friberg describes 50 cases of "metal-fume fever" occurring in a large industry in Sweden. The workmen affected were cleaning copper dust from a plant and the particle size was of the order of 1 to 15 μ.

A detailed review of the effects of copper is contained in an article entitled "Copper and Health" (*Industr. Med.*, 1947, **16**, 368).

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Occupation and Health, International Labour Office, Geneva, 1930, **1**, 501.
Schiötz, E. H., *Tidsskr. norske Lægeforen.*, **67**, 451; Abstr. *J. industr. Hyg.*, 1948, **30**, 10.

Hydrocele in Children

Q.—*At what age should a hydrocele be treated, and how? A boy of five, the younger of dissimilar twin boys, has a left hydrocele. It varies in size up to that of a ping-pong ball.*

A.—The hydroceles of infancy and early childhood are of various types depending upon the degree to which the normal obliteration of the funicular process fails to take place. The so-called congenital hydrocele in which a communication still exists between a completely patent funicular process and the peritoneal cavity is really a hernial sac with a narrow neck and no contents (other than serous fluid). It will usually require operation, though there is no urgency about this unless there is a large amount of fluid in the hydrocele. In such cases a low-grade tuberculous peritonitis should be suspected. Between five and seven years of age is a reasonable time for surgery.

The "infantile hydrocele" (when the neck of the otherwise patent funicular process is sealed off from the general peritoneal cavity) and the "encysted hydrocele of the cord" (a localized patent part of the funicular process) are both best treated by simple aspiration, repeated if necessary, and pressure. Repeated recurrence calls for operation—again at about five to seven years of age. However, children do develop genuine vaginal hydroceles and here the question of pressure on a soft developing testis has to be considered. Aspiration alone is successful in 75% of cases, but recurrence or continuing discomfort will demand operation. If the child is otherwise fit, no purpose is served by delaying operation. The case in point seems to be of this type and the hydrocele should be aspirated once or twice before surgery is considered.

Manganese Poisoning

Q.—*What are the signs and symptoms of manganese poisoning? Is this likely to arise in workers who are engaged in ore welding in a confined space? Is there any treatment and what are the appropriate methods of prevention?*

A.—The crushing, grinding, and sieving of ores containing manganese dioxide expose workers to dust, and it is from exposure to these processes that the majority of cases of manganese poisoning have arisen. Manganese dioxide is used extensively in the manufacture of dry batteries, also in the manufacture of glass. It has been stated that in the smelting of iron ore containing considerable quantities of manganese, cases of poisoning among furnace workers may occur (Legge). To these occupations should be added that of welding manganese alloys. The characteristic signs and symptoms of manganese poisoning are: a stolid mask-like face and low monotonous voice; cramp in the legs with muscular twitching, increased tendon reflexes, ankle and patellar clonus; retropulsion and propulsion, a peculiar gait described as slapping, the patient walking on a broad base; and emotional disturbances, occasionally uncontrolled laughing or crying. Serious poisoning produces crippling effects. The first evidence of ill-health due to exposure to manganese dust or fume may be nocturnal cramps in the legs, followed by indigestion, nausea, vomiting, and anorexia. The respiratory system may also be affected and illness of a bronchitic, bronchopneumonic, or pneumonic type may ensue. Lloyd Davies has recorded that "people unused to exposure to manganese dust notice an irritation of the nose shortly after exposure; some hours later the nose feels blocked and epistaxis may occur." Treatment is symptomatic, with avoidance of further exposure, while prevention lies in adequate and effective means for the removal of dust and fume from the working environment.

NOTES AND COMMENTS

Copra Bug.—Dr. I. G. CAMERON writes from Nairobi: In your issue dated October 22, 1949 (p. 939), under the heading "Any Questions?" the answer given to an inquirer is that the copra bug is a species of mite, *Tyrophagus castellani*. While there is a mite that may cause skin irritation, the insect commonly known as the copra bug is quite different. It is a small dark brown flying insect which bites readily and is a perfect nuisance on board cargo ships from the Far East which carry copra. Recently cured copra harbours many more of these insects than older copra that has been lying in a godown for some months. On board ship these insects are ubiquitous. They are found in one's soup, in one's bread, and in one's cabin at night. Unless one has a careful search each night before retiring and kills every one of them in the cabin, one is wakened many times by the sharp nip that these creatures are capable of giving. When the hatch covers are opened for ventilation, as usually happens in the Red Sea, they fly out in their millions. By the time the ship gets into a colder climate most of them have either been blown off the ship or have died, but some survive to annoy the dockers. It is impossible to disinfest the copra with D.D.T. or some such insecticide, for the copra is carried in bulk, loose in the hold, and such disinfestation would make it unsuitable for use for margarine or other food products. Also the amount of insecticide necessary would be enormous, when one realizes that some ships carry 5,000 tons of bulk copra. As to applying dimethyl phthalate to the skin each day to try to prevent the insect from biting, I would like to see the docker who would be bothered. Certainly one never bothered on board ship, nor did the crew ever come to me with any such trivial complaint.

Vasomotor Rhinitis.—Dr. T. B. JOBSON (Guildford, Surrey) writes: In a question on vasomotor rhinitis ("Any Questions?" December 10, p. 1365) it is mentioned that the diagnosis of a nasal polypus was made on an *x*-ray finding. May I point out that this may be an incorrect conclusion? I have had several cases in which a second radiograph revealed that the shadow polyp had completely disappeared. In one case a Caldwell-Luc operation was done, but no polyp was found. Discussion with the radiologist caused us to come to the conclusion that these shadows are caused by a localized oedema in an allergic subject and are of a temporary nature. True antral polypi are usually the result of long-standing septic sinusitis of the antrum.

National Television Fund.—The Secretary of the National Television Fund writes: Some of us have already been able to enjoy the pleasures of television, but many sick or crippled children and many old folk during the closing days of life condemned to some chronic disability may never have the chance of availing themselves of this new and modern delight. To meet this need the National Television Fund has been set up for the purpose of providing suitable sets for presentation to hospitals and other charitable institutions maintained for the welfare of both young and old. Already some of these we have in mind have been able to equip themselves with excellent sets, but it has not been possible to do so in the vast majority of cases. May we ask for subscriptions and donations, which will be most gratefully acknowledged, and should be addressed to the National Television Fund, 12, Whitehall, London, S.W.1.

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